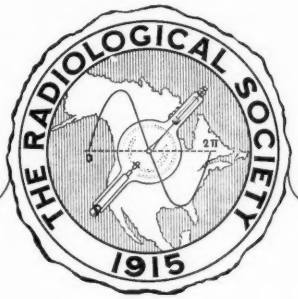
RADIOLOGY

A MONTHLY JOURNAL DEVOTED
TO CLINICAL RADIOLOGY AND
ALLIED SCIENCES



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VOLUME XXII NUMBER 1

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PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

VOL. XXII JANUARY, 1934 No. 1

CORRELATION OF CLINICAL AND ROENTGENOLOGICAL OBSERVATIONS IN PULMONARY TUBERCULOSIS[1]

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INTRODUCTION

MAY we express to you our keen appreciation of the honor we have received in being asked to address this Congress. We come to you with feelings of deep gratitude for the help that we have received from many of the members, men who started us on our way when we began our work, among many others Cole, Dunham, Pancoast, and our life-long friend Harry Baetjer. We have followed the roentgenologic study of the lungs from the time when Blake found an exposure of eight hours necessary in order to get a picture of the bronchi filled with Wood's metal until the present time, when many consider one-fifteenth of a second an over-exposure for a lung film. We wondered, in 1907, at Cole's ability to state that disease existed in a certain portion of the lung, where a little later we heard râles develop. To-day we have progressed to the stage were we call no man sound pulmonically until his stereoscopic roentgenograms have been found to be normal, and consider the roentgenologic study as much a part of the routine examination of the lungs as the stethoscopic, or, indeed, as the examination of the sputum. We, too, have stood the jeers of some of our confrères for our faith in the roentgenogram but have watched many slowly accept this point of view. We have seen the belief that pulmonary tuberculosis begins at an apex replaced by the opinion that it arises at the hilum, which is now—from further roentgenologic study—also abandoned. We have combated the view that physical signs were precise enough for use in classification and insisted upon what, then, was considered too radical a view—that as a basis for classification the roentgenogram must replace physical signs for the sake of accuracy. This, as you know, has come to pass. We have seen thoracic surgery attain the advanced position it occupies to-day, due solely to the precise diagnosis of the extent of the pulmonary lesion made possible by a roentgenologic study. The significance of the pulmonary roentgenogram in pulmonary tuberculosis is better appreciated when we recall that 88 per cent of all patients with tuberculosis are said to have the disease in their lungs, from which 15 per cent die, 15 per cent recover, and 70 per cent remain unaware of the presence of the more or less important lesion. But even this is not all. The pathologists have adopted the technic of Dunham and have at autopsy removed the lungs from the thorax, inflated them to their usual size, and then radiographed them in order to discover in this way, and only in this way, certain finer pathologic changes. We cannot for-

[1] Read before the American Congress of Radiology, at Chicago, Sept. 25–30, 1933.

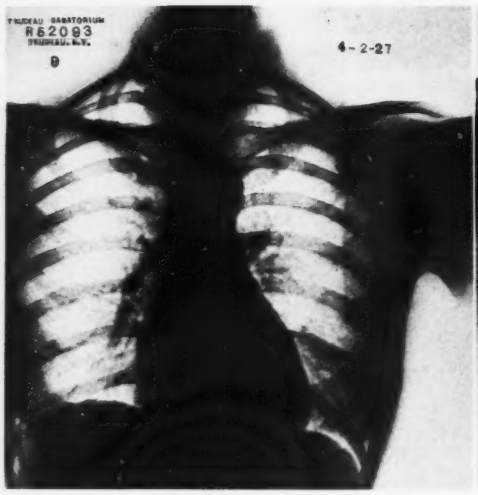


Fig. 1. Physical signs more than x-ray findings: bacilli negative. Physical signs: left lung, moderately coarse râles throughout. X-ray findings: left lung, small amount of infiltration to second lobe on the right.

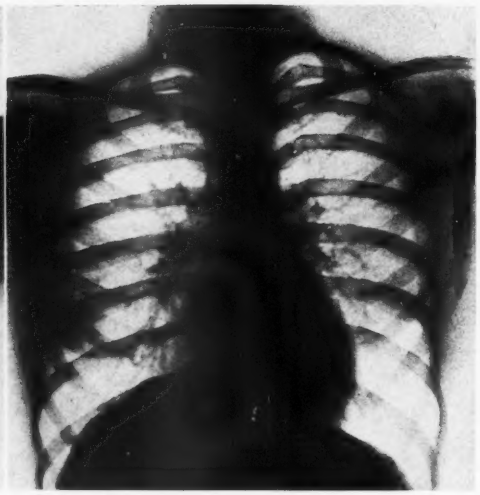


Fig. 2. Physical signs positive, x-ray findings negative: bacilli negative. Physical signs: right lung, moderately coarse râles to third rib; left lung, moderately coarse râles to third rib. X-ray findings: negative.

bear suggesting that the roentgenograms may be likened to a pulmonary biopsy and, while a pathologic study of any given lung is limited, of course, to a single state, in a series of roentgenograms we have serial biopsies on lesions in a state of flux. These studies have greatly helped to banish ennui from the sanatorium. But, gentlemen, this stampede to roentgenologic study—to the roentgenogram—has brought with it certain responsibilities which must fall upon your shoulders. We refer to the necessity of stressing the value of the former methods of pulmonary physical diagnosis, which for many, many reasons cannot be safely neglected.

DIAGNOSIS

Any study of a comparison of the relative value of the findings obtained from the usual physical examination and from the roentgenologic examination suggests an immediate comparison of the more advanced patients. Before taking this up we would like to call to your attention the great importance of the detection of two intrapulmonary pathologic changes. We refer to the discovery of the earliest lesion of pulmonary tuberculosis and of the presence of any degree of cavitation, which is so important in treatment. It seems hardly necessary for us to repeat that primary infection in infancy or childhood, producing a small patch of bronchopneumonia, cannot be diagnosed by physical signs and is rarely detected save by accident even by roentgenology until such time as it has been apparently healed and calcified or ossified. The same thing is true of the associated changes in the tracheobronchial lymph glands, which entirely escape detection by physical examination and are not seen roentgenographically until such time as they project their shadows into the high light of a bronchus or into the normal roentgenologic field. D'Espine's sign has been shown by roentgenographic study to be of no value. The importance of the discovery of the primary infection is attested by thousands of dollars which have been spent during the last one or two decades for roentgenologic investigation, which alone localizes in the lung an infection

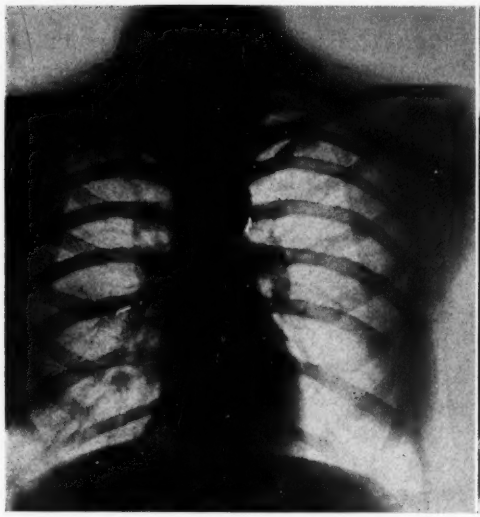


Fig. 3. Physical signs positive: bacilli negative. Physical signs: right lung, breathing broncho-vesicular, vocal resonance increased and râles to third rib. X-ray findings: negative.

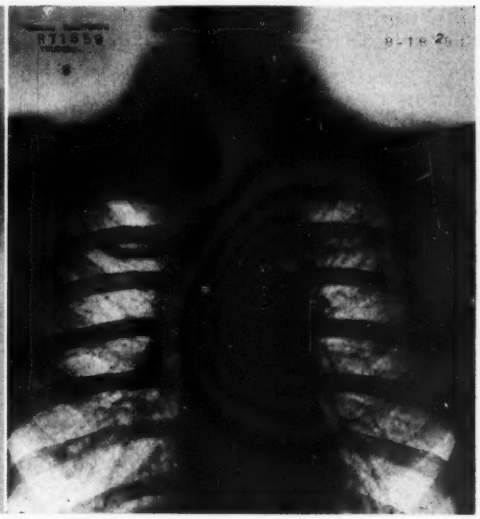


Fig. 4. Illustrative of the absence of physical signs of cavity in the presence of large bilateral apical cavities: bacilli Gaffky X. The physical signs present were moderately coarse râles in the upper half of each lung with impaired note on the right.

suggested by a positive tuberculin test. Physical signs tell us little of what happens in regard to tuberculosis in the lungs during that period when the disease exacts its least toll in human life. We refer to the interval between the time when the primary infection usually occurs and the development of definite adult pulmonary tuberculosis, possibly from the age of six or seven to puberty. Whether adult pulmonary tuberculosis is due to a hematogenous infection arising from the primary focus, or (as is now commonly assumed) from a re-infection upon a sensitized soil, will have to be solved later and roentgenology will play no small part in it. We feel that so far roentgenology has given some proof, lacking, of course, to physical signs, that the adult type as a rule does not arise directly by extension from the primary lesion. We base this upon our own observations and, furthermore, upon roentgenologic studies of the location of the primary lesion which has been shown to occur in a vast majority of cases in the lower lobe (77 per cent) and in the right lower lobe in 67 per cent of all cases in one study (Heilig).

The time is now upon us in the prevention of tuberculosis when it will no longer do for us to wait for the development of clinical pulmonary tuberculosis before attempting to control it. We must discover which individuals have definite pulmonary lesions and endeavor so to direct their lives that the disease, undiscoverable by physical signs, to be revealed only by roentgenology, may make no further advances. We feel, furthermore, that, if by the age of 23 there are no parenchymatous changes in the lung suggestive of pulmonary tuberculosis, only in rare instances, and then usually only when subjected to repeated and continuous infection, will the individual develop pulmonary tuberculosis. To carry this further back, recognizing for a long time the futility of physical examination in discovering such lesions, we have advocated for years that no child be allowed to leave school, and particularly high school, until a roentgenologic examination has been performed. This, we feel, would reveal

the great majority of those who during the second, third, and fourth decades of life are likely to break down with clinical pulmonary tuberculosis, requiring strenuous and prolonged treatment. With Dr. Haskins, we have studied roentgenologically all the school children of Saranac Lake for the past seven years, numbering over 4,000. Of those showing parenchymal lesions and who had a physical examination, numbering 79, only 7 had definite physical signs.

MINIMAL PULMONARY TUBERCULOSIS

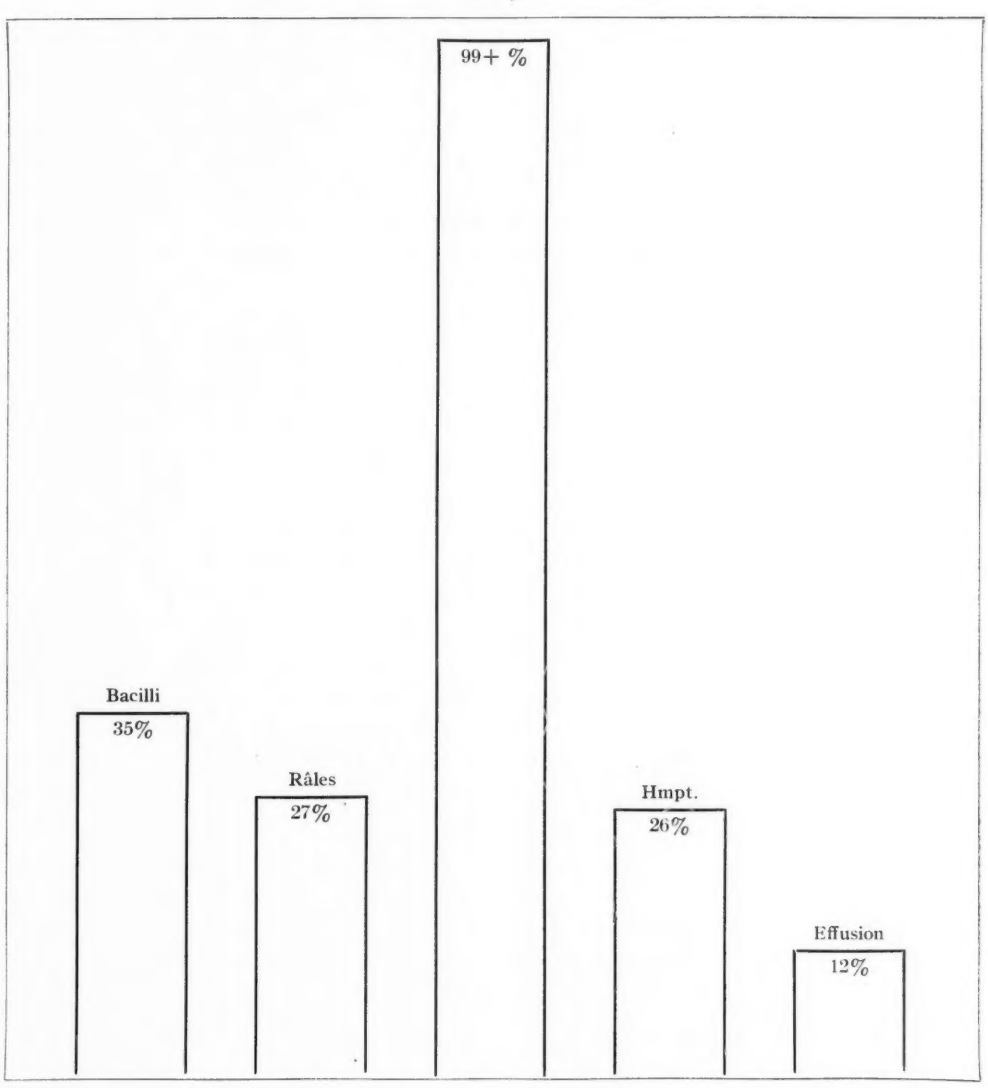
In spite of Fowler's assertion that the usual site of beginning pulmonary tuberculosis is under the clavicle, for years the idea that it began at the very apex of the lung was commonly accepted. The reason for this was the fact that slight changes in breathing (roughened breathing, prolonged expiration), possibly a slight increase in the vocal resonance, together with some more or less fancied change in the percussion note, did occur at the apex in some patients who later developed a fatal pulmonary tuberculosis. Many of these individuals were sent for treatment to the sanatorium where they helped swell the favorable statistics. Protests were uttered, and at the Trudeau Sanatorium we endeavored to meet the criticisms by giving every patient who had no tubercle bacilli in his sputum the subcutaneous tuberculin test. This was, however, far from satisfying. Indeed, the whole subject remained in a fog until such time as roentgenology cleared it up. The roentgenogram revealed to us that the usual site of beginning clinical pulmonary tuberculosis was in the upper lobe below the clavicle and the slight changes noted above were due to lesions—deep seated in some cases, in others healed—or, indeed, to no definitely determined pathologic changes and consequently of no moment.

It is of some interest to note the findings in 280 patients with minimal pulmonary tuberculosis. This group, you will recall, includes all those with the slightest but still sufficient evidence on which to base a diagnosis of beginning pulmonary tuberculosis. After careful consideration the staff at the Trudeau Sanatorium came to the conclusion some years ago that moderately coarse râles at an apex were the only reliable data obtained on physical examination. In these 280 patients, such râles were present in 27 per cent, while a definite parenchymatous roentgenologic lesion was found in over 99 per cent. Hemoptysis was as frequent as râles (26 per cent), while pleuritic effusion occurred in 12 per cent. Tubercle bacilli in the sputum were found in 35 per cent. When in any group of 280 patients, 277 have definite roentgenographic evidence of pulmonary tuberculosis and only 76 present definite evidence of physical signs, the relative value of the two methods in minimal pulmonary tuberculosis needs no further discussion.

In still another attempt to compare the relative values of physical signs and roentgenographic findings, 1,004 consecutive patients were studied, and the results are most interesting. In the first place, there was none with definite physical signs and a negative roentgenogram. In 19, the physical signs suggested a greater extent of the lesion than the roentgenogram. In 211, the extent was equal by both methods. In 361, the roentgenogram revealed more extensive disease than was inferred from the physical signs. In 396, the roentgenogram showed definite evidence of pulmonary tuberculosis, while the physical signs were practically normal. If we can assume that the presence of cavity indicates a greater intensity of the disease, the roentgenogram again is far more accurate, for in 392 patients with cavity, only 58 (15 per cent) had physical signs suggestive of cavity. (See Diagram II.)

In a study of 1,367 patients diagnosed as having pulmonary tuberculosis, a comparison of the physical and roentgenologic findings brought to light that, while 68.5 per cent of them had definite râles at an apex, over 99 per cent had definite roentgenologic changes. It is of some interest

DIAGRAM I.—INCIDENCE OF THE FIVE CARDINAL SYMPTOMS IN 280 CASES DIAGNOSED AS MINIMAL TUBERCULOSIS



to record the occurrence of the other cardinal criteria; tubercle bacilli, 61.5 per cent; hemoptysis, 33.5 per cent; pleuritic effusion, 12 per cent.

Several years ago one of us (L. B.) published a "blast" against the skeptics who, we considered, were unnecessarily belittling the value of the roentgenologic study in cases diagnosed from the roentgenogram as having pulmonary tuberculosis. From a study of 503 patients whose lungs presented only indefinite or no abnormal physical signs, we were able to show that sooner or later over 84 per cent presented clear-cut clinical evidence of the disease. (See Table I.)

TABLE I.—503 CASES WITHOUT PHYSICAL SIGNS

	Bacilli Plus	Râles Later	Hemoptysis	Effusion	Relapsed	Dead	Local Symptoms	Arrested Pul. T.B.	General Symptoms
Min. 159	52	12	34	10	11	4	26	6	4
M.A. 322	226	23	29	10	10	4	17	2	1
F.A. 22	20	1				1			
	298	36	63	20	21	9	43	8	5

Several studies of groups of patients whose roentgenograms showed no evidence of a parenchymatous change interpreted as tuberculous have been studied. In 264 patients (Brown and Heise), in whom none of the five cardinal diagnostic criteria was present, followed after one to seven years, only two developed pulmonary tuberculosis and one of these had a carious rib and the other had tuberculous cervical adenitis at the time of observation.[2] Another study of 2,600 consecutive cases showed 298 with negative roentgenograms and revealed that only two of these patients developed and died from tuberculosis. It is of interest to record that while in 1916, 14.6 per cent of patients with negative roentgenograms were admitted, in 1932 the number had fallen to 4.5 per cent. From this we are led to conclude that, while formerly many patients with very equivocal signs were sent to the Trudeau Sanatorium with a diagnosis of pulmonary tuberculosis (for they were all thus diagnosed before admission), to-day the more extended use of the roentgenogram has greatly reduced the percentage.

Another study of 312 patients without definite roentgenologic change presenting one or more of the other four cardinal diagnostic criteria revealed that 59 were said to have had tubercle bacilli in the sputum at some time, often before admission, 81 râles at the apex, 68 râles at the base, 76 hemoptysis, and 28 pleural effusion. Of these, two died, one of whom had been reported as having had tubercle bacilli in the sputum, the other as having had hemoptysis.

[2] The five cardinal diagnostic criteria are tubercle bacilli, moderately coarse râles above the third rib and third vertebral spine, a parenchymatous roentgenologic lesion in the same area, hemoptysis, pleurisy with effusion.

In a study of 1,000 patients at the Trudeau Sanatorium, Heise and Brown concluded that râles lose in diagnostic significance as they occur in isolated areas from the upper third of the lung downwards. Moderately coarse râles in the upper third of the lung are associated with a positive roentgenogram in 98 per cent, fine râles in the same location in 80 per cent. In 20 per cent of the patients in this group with positive roentgenograms, no râles were heard.

The incidence of a parenchymal lesion in those cases having bacilli was 99.2 per cent; with râles in apex 99.3 per cent; with hemoptysis 96.1 per cent, and with pleurisy with effusion, 98.5 per cent. The fact that only 96 per cent of those giving a history of hemoptysis had a parenchymal lesion, makes one wonder whether the "hemorrhage" came from the lung.

Such observations as these are not exceptional. Plunkett, Miller, and Hamon, Barnes, Soper, and Wilson, John Tillman, Loose, Becker, and others, have all expressed more or less similar opinions.

We would not have you believe, however, that physical signs can be safely omitted. The absence of liver dullness in the lower part of the right chest suggests pneumothorax in the absence of an abnormal abdominal condition, and dullness over Traube's semilunar space may be helpful even in interpreting a roentgenogram.

CLASSIFICATION

The classification of pulmonary tuberculosis has long been a stumbling block to the sanatorium physicians. The earliest systems abroad were based entirely upon a study of the physical signs, but sooner or later they were recognized as unsatis-

DIAGRAM II

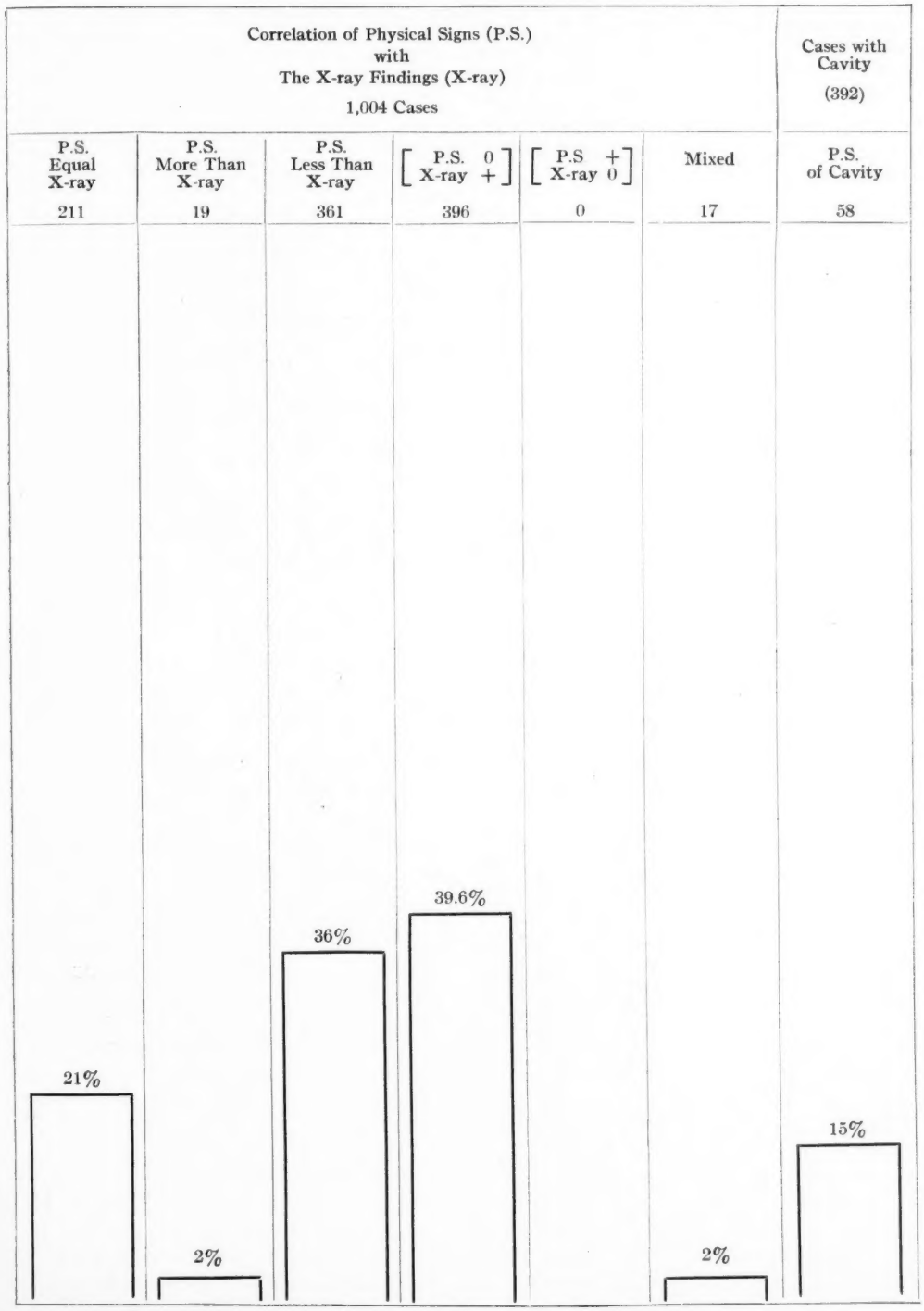

Correlation of Physical Signs (P.S.) with The X-ray Findings (X-ray)
1,004 Cases
Cases with Cavity (392)
P.S. Equal X-ray
211
P.S. More Than X-ray
19
P.S. Less Than X-ray
361
P.S. 0 X-ray +
396
P.S + X-ray 0
0
Mixed
17
P.S. of Cavity
58
21%
2%
36%
39.6%
2%
15%

TABLE II.—RECLASSIFICATION OF 1472 CASES

73 Non-tuberculous	120 Suspects		392 Minimal		809 Moderately Advanced		78 Far Advanced	
		Per-centage		Per-centage		Per-centage		Per-centage
Remained the same	N.T. 85	71.0	N.T. 98	26	N.T. 26	3.0		
	Sus. 18	14.9	Sus. 43	11	Sus. 20	2.5		
	Min. 16	13.3	Min. 134	33	Min. 123	15.0		
	M.A. 1	0.8	M.A. 109	28	M.A. 621	77.0	M.A. 15	20
			F.A. 8	2	F.A. 19	2.5	F.A. 63	80

factory. In this country both symptoms and physical signs were taken into consideration. Some fifteen years ago the American Sanatorium Association appointed a committee to report upon the subject, which committee suggested that the classification should revert to one based upon physical signs. One of us opposed the report and submitted a minority report suggesting that, as physical signs were notoriously uncertain in determining the extent and intensity of the disease, we should use the roentgenologic examination as well. You know what has happened. Physical signs have been abandoned and to-day the roentgenogram reigns supreme, as we urged. It is of some interest for this as well as for other reasons to compare briefly the findings in pulmonary tuberculosis obtained from the physical signs and the roentgenogram.

In the study of 1,004 patients which we have mentioned, you will recall that there was no instance wherein the physical signs were positive and the roentgenogram negative for pulmonary tuberculosis; in 2 per cent the physical signs indicated a greater extent of involvement than the roentgenogram; in 21 per cent the extent of disease as indicated by each was the same; in 36 per cent the roentgenogram revealed more extensive disease than the physical signs, and in 39.6 per cent the roentgenogram showed involvement while the physical signs were apparently normal. All future classifications must at least take the roentgenogram into consideration if they are not to be based largely upon it.

Some years ago before one of your component bodies we reported the results of the re-classification of some 1,472 patients, who previously had been classified by symptoms and physical signs. Of the 120 "suspects" of the original classification, only 15 per cent remained in this group, while 71 per cent were found to be "non-tuberculous," and 13 per cent "minimals." Of the previous "minimals," 33 per cent remained in this group, 26 per cent were transferred to the "non-tuberculous," 11 per cent to the "suspected," and 28 per cent to the "far advanced." The "moderately advanced" group was the least affected, but 20 per cent of the "far advanced" were transferred to the "moderately advanced." This needs no comment. Physical signs alone or grouped with symptoms constitute a fallacious basis for classification. The roentgenogram alone is sufficient. (See Table II.)

When we consider the condition of the patient at any time toward the end of treatment, we are again confronted with a similar condition. Physical signs fail to tell the true condition of the patient which is more accurately revealed by the roentgenogram. Here serial roentgenograms are of great importance, for the disease is not truly arrested until changes in the roentgenogram for better or for worse no longer occur. This slow improvement of the condition, covering in certain instances a period of several years, has explained why some patients suffer relapse when apparently from the symptoms and physical signs they are doing so well. The disease is still potentially active and slight indiscretions may sooner or later bring about relapse.

Pathologists have attempted to classify pulmonary tuberculosis according to certain types, the best known having at one extreme the acute exudative type (bronchopneumonia), at the other the fibrous scar

or calcified nodule. To attempt this during life from a study of the physical signs is futile, but the roentgenogram does afford help and from its study we are enabled in some instances to state whether a proliferative or an exudative lesion preponderates in certain areas of the lung. Again, the physical signs of miliary tuberculosis are notoriously indefinite, while the roentgenogram lays bare the condition. We would like again to call to your attention Cole's very ingenious classification, published some years ago.

CAVITY

In no pulmonary lesion does roentgenologic study give greater assistance than in the detection of an intrapulmonary cavity, which naturally lends itself to such study. In the Trudeau Sanatorium, where for many decades patients with cavity detected by physical examination have been excluded, it is of interest to note that over 40 per cent of the patients have cavities when studied roentgenologically. In a series of 392 consecutive patients with cavities, clearly shown on the roentgenogram, in only 15 per cent were there any physical signs even suggestive of cavitation. In another more recent study of 500 patients with cavity, the classical physical signs interpreted as definitely indicating the presence of cavity were present in only 5 per cent.[3] The detection of cavity by physical signs depends upon the size and location of the cavity and the increased density of the lung between the cavity and chest wall. If the bronchus draining the cavity be closed by secretion or by twisting or stenosis, the cavity is silent.

That fluid levels do occur in cavities all acknowledge, but that Gerhardt's sign could occur is almost inconceivable save in giant cavities. Wintrich's sign affords little help, roentgenologic study shows. Spurred on by the presence of large cavities in parts of the chest that apparently are accessible to detection by physical signs, some would have us accept what they call suggestive signs of vomica, *e.g.*, broncho-vesicular breathing, harsh inspiration with coarse, moist, bubbling râles over a limited area below the second rib, or, again, even the râles alone below the clavicle when associated with a stormy course. But here again roentgenologic examination is urged (Debove, Dunham). Signs of cavity in the inner first interspace frequently occur when the trachea is drawn markedly to one side. This error, as Webb has pointed out, can be avoided by noting the position of the trachea by palpation or on the roentgenogram.

In 145 cavities, detected by roentgenologic study, 45 per cent had physical signs of cavity and 66 were without the classical signs, in a study by Burns and Carrard. In this group, 42 were absolutely silent. They thought that obscured breathing in a suspected area was most suggestive. Fales is also of the opinion that over 50 per cent of all cavities are silent, and he found that in 245 patients, 90 (36 per cent) had cavity but only 20 presented at least two of the criteria diagnostic of cavity. Ulrici estimated that over one-third of all cavities are silent.

It must be regretfully confessed that the vast majority of all pulmonary cavities are "silent" and some also are invisible. Unfortunately again many cavities do develop when the patient is undoubtedly improving symptomatically and for months may remain silent.

We have made a study of that type of cases which Archibald has called "good chronics." These patients must be in good general condition with good strength, have a normal temperature and pulse, tubercle bacilli usually present in the sputum, but the condition of the lungs must show an advanced stage of tuberculosis. Here, again, the physical signs are inadequate in the majority of the cases

[3] The classical physical signs indicative of cavity include the following: tympanitic or cracked-pot note, markedly increased vocal resonance (intense bronchophony, pectoriloquy), amphoric or bronchial breathing, coarse, consonating, metallic, bubbling râles.

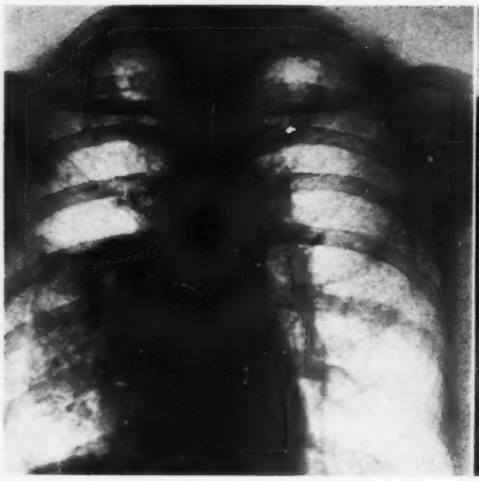


Fig. 5. Physical signs essentially negative: bacilli Gaffky VII. Physical signs: right lung, breathing broncho-vesicular, vocal resonance increased, no râles. X-ray findings: moderately to far advanced.

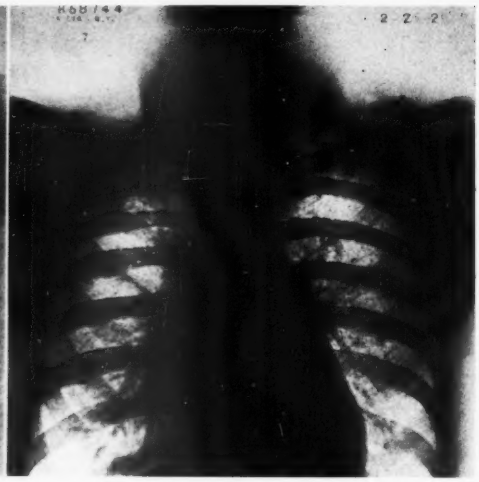


Fig. 6-*A*. Bacilli Gaffky VI, illustrating the disappearance of physical signs *versus* an increase in size of cavity as revealed in roentgenogram. Admission physical examination: right lung, râles to third rib, breathing broncho-vesicular and vocal resonance increased, also impaired note to clavicle and 3 V.S.; left lung, impaired note to clavicle and 3 V.S. X-ray findings: right lung, infiltration to third rib; cavity in apex.

to portray the actual pulmonary condition, and once more we must turn to the roentgenologic examination. The details of this study will be published elsewhere but we might say that, selected in this way at the end of ten years, 52 per cent of the "good chronics" are living and working, 34 per cent are dead, while for the "bad chronics" the corresponding figures are 11 per cent and 76 per cent. We might add that all these patients on roentgenologic examination had pulmonary cavity.

ACTIVITY

We have defined pathologic activity as that stage of a tuberculous process in which some change is taking place, whether progressive or retrogressive. Clinical activity, we hold, is that state in which the pathologic activity is not latent, but produces (through actual and immediate absorption of poisons) certain clinical or laboratory manifestations of disease, which disease may in turn be progressing, stationary, or even for the time retrogressing. In other words, activity implies disease which is in a state of actual or potential increase or decrease in extent or intensity, or, indeed, in both. Repeated examinations by the usual means of physical exploration or by roentgenograms indicate in many of these patients an increase of physical signs or of the shadows. It has long been recorded by one of us (L. B.) that an increase in the physical signs may accompany a very definite improvement in the clinical condition, which, years ago, led us to question the reliability of increasing physical signs as evidence of an advance of the disease. Not until the advent of the "pulmonary biopsy," as we call the roentgenogram, could we obtain data which helped solve this problem. A comparison of physical signs and the roentgenogram showed that in such instances there was frequently a decrease of the pulmonary shadows, interpreted by us as a decrease of the pathologic process. Further interesting data came also to light. The physical signs in a number of cases remained the same, while the roentgenographic evidence

of disease showed a very definite increase. On comparison of serial roentgenograms, few question the evidence of activity based upon the observation of new "daughter" foci, as we may term the perifocal increase of shadows.

The subject assumes an entirely different aspect if we attempt to determine activity from a single examination by physical exploration or from a single set of stereoroentgenograms. I have often recalled what Dr. E. L. Trudeau once told us. If he were led blindfolded, he said, to a patient and permitted to examine him only with his stethoscope, he would have great difficulty in deciding whether the patient was soon to be gathered to his fathers or in condition to return to work—probably an over-statement for emphasis of an important fact. Without doubt there are some râles that suggest activity, bubbling, consonating, and particularly crepitant, the last of which are so rarely heard in pulmonary tuberculosis that they are of no help. No other physical sign is of significance in the determination of activity. When we turn to the single set of stereoroentgenograms we have a very difficult and perplexing task in trying to determine activity. Here we must ever keep in mind that a small focus of active disease may be invisible, though, as a whole, the lesion may be inactive. It is likely that there is no problem connected with activity in which the personal equation enters so largely, and yet a fair estimate may usually be made after some practice with good, rapidly exposed roentgenograms. Certain shadows with ill-defined borders, suggest to us activity, while those with clear-cut borders indicate an inactive condition. We have attempted to correlate these interpretations with what happened to 1,024 consecutive patients during their residence in the Trudeau Sanatorium. Of them, 434 (40.5 per cent) were classified from a study of the roentgenogram as active, and in 63.3 per cent of these subsequent roentgenograms revealed progression of the disease or artificial pneumothorax was administered. No attempt was made to determine activity from the physical signs, but 294 (30 per cent) were regarded symptomatically as active and of these 52 per cent later showed a definite advance of the process. Of 125 patients who later relapsed, 88 per cent had been diagnosed as active from the roentgenogram, 45 per cent from symptoms.

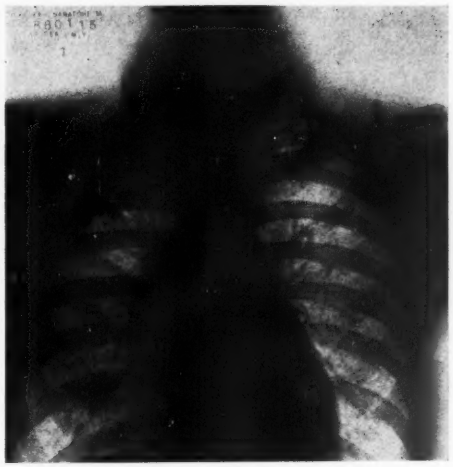


Fig. 6-*B*. Discharge examination: physical signs—right lung, impaired note to clavicle and 3 V.S., no râles. X-ray findings—right lung, increase in size of cavity.

Such evidence, we feel, points to the conclusion that the roentgenogram is vastly more important in the determination of activity than the physical signs.

PROGNOSIS

From what we have said it is correct to infer that we place great significance upon the roentgenogram in determining the prognosis. The undue weight that the presence of a cavity lends to the prognosis amply justifies such a statement. Furthermore, the seriousness of the cavity depends in no small part upon the condition of the disease surrounding it, and this is revealed only by the roentgenogram. If Pirie be correct in his suggestion that the heart muscle atrophies relatively more than the other muscles,

and we all are aware of how much they atrophy, then special roentgenograms are again of much help.

TREATMENT

For over a hundred years students of pulmonary tuberculosis have turned to the study of the physical signs in an attempt to determine the course of the disease, and hours of painstaking endeavor and pages of description of minute differences in questionable data have resulted. In a great number of patients the physical signs showed no change, while the patient improved markedly in every other way. In a certain number the signs decreased while the patients apparently grew worse. In others, the physical signs increased while the patients evidently improved. However, in a considerable number changes in both physical signs and improvement went hand in hand. Another condition has long troubled the clinician. As everyone knows, pulmonary tuberculosis in many patients neither advances nor retrogresses steadily but does so by sudden changes. They suggest steps with wide treads and slight rises or falls, as you will. The usual picture is one in which the maximum temperature increases slightly for several days and slight or moderate increase of symptoms takes place. Possibly the patient is thought to have a cold. Physical examination reveals no changes and the clinician is left in doubt in regard to what has happened and concerning how much rest he should prescribe. We can speak feelingly, for we have had to face this problem for over thirty years. It is impossible for anyone who has begun the study of pulmonary tuberculosis only since the time when the roentgenogram has become widely used to appreciate our former state of mind. The dreadful uncertainty, the impossibility of saying whether the patient was better or worse, whether the little upset was due to an advance of the disease or to an intercurrent cold has now been almost entirely removed by the roentgenologic study. Serial roentgenograms enable us to quiet the fears of many patients, to return others to prolonged rest with marked benefit, and, what is of no little importance, to remove that dreadfully distressing state of doubt—and later of remorse—for making a wrong guess. We are convinced that many of the phthisiologists have come to the conclusion that in regard to the study of the physical condition of the lung in tuberculosis the roentgenogram far excels any and all data obtainable from the usual methods of physical exploration. And, yet, gentlemen, for this very reason it seems to me that you have before you a very clear duty. You must stress the value of the physical examination whenever the opportunity occurs, for you have now the whip hand.

COLLAPSE THERAPY

It seems rather useless to compare the value of physical signs and roentgenologic study in collapse therapy. Here precision of diagnosis is highly important and the data recovered from physical signs too uncertain. We are free to confess that we would not abandon artificial pneumothorax even if we had no x-ray machine, but we would doubtless, when basing our decision entirely upon symptoms and physical examination, overlook many patients who required such treatment and administer it to others who did not need it. When once begun, artificial pneumothorax so changes all physical signs that even those most expert with physical examination are often left in a maze of doubt and uncertainty. When to give refills can be gauged with a certain degree of accuracy by the recurrence or increase of symptoms, but the last word is spoken by the fluoroscope or roentgenogram. The former enables us to postpone many refills or, more rarely, urges us to decrease the intervals. When the lung is once completely separated from the chest wall physical examination, save for the detection of fluid, is of little moment. Under these conditions cavities may still be held

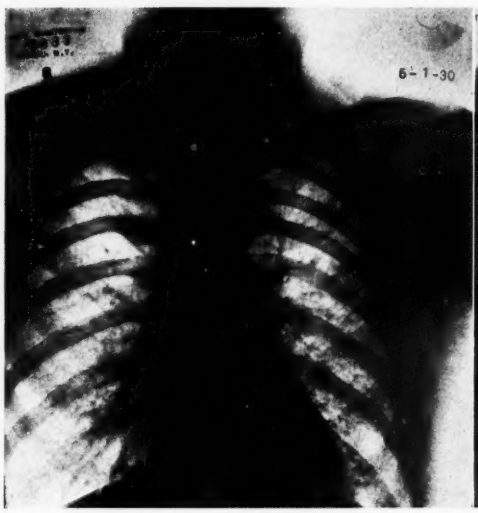


Fig. 7-*A*. Illustrating physical signs worse, x-ray better: bacilli Gaffky II. Physical signs: admission examination, right lung, fine râles to clavicle; left lung, moderately coarse râles and impaired note to third rib. X-ray findings: admission examination, right lung, infiltration to clavicle; left lung, infiltration throughout.

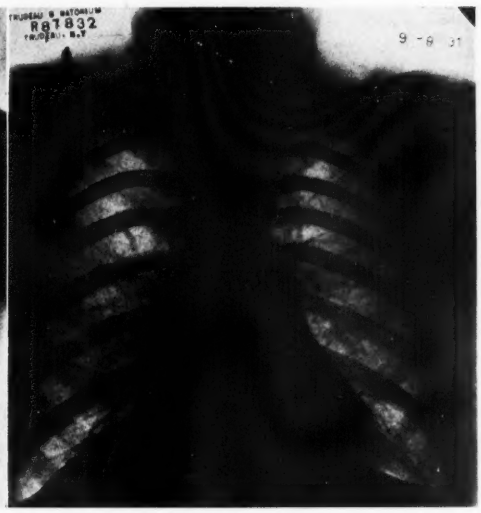


Fig. 7-*B*. Physical examination: right lung, negative; left lung, râles throughout. X-ray findings: right lung, infiltration to clavicle; left lung, marked clearing of infiltration in the lower half.

open by adhesions, and roentgenologic study alone discloses it.

It might be possible to practise intrapleural pneumolysis without the roentgenogram, but we would hate to do so. Apart from artificial pneumothorax, operation upon the phrenic nerve has become the most common procedure in collapse therapy. We cannot picture recommending this operation except after roentgenologic study for the physical examination is of little help. For the best results it is necessary to make certain that the cavity is thin-walled, that the lung is attempting to contract as evidenced by a shift of the mediastinum toward the cavity-containing lung, by a narrowing of the interspaces and a rise of the diaphragm. Only roentgenologic study yields accurate information along these lines.

The detection of a movable, shifting mediastinum may present no physical signs of its presence and even the so-called mediastinal hernia follows the same rule. The extent of compression at any time is most easily determined by roentgenologic examination and when the lung is being allowed to re-expand and some anxiety exists as to whether or not it is safe to cease artificial pneumothorax entirely, whether or not a previous cavity has remained closed, only a roentgenogram will give sufficiently accurate information. After the cessation of artificial pneumothorax it may become most important to be able to note if the collapsed lung is really expanded or merely shifting toward the lateral wall. This information must be obtained in a similar manner, as well as suggestive data regarding the occurrence of a superimposed rupture. When the smooth homogeneous highlight or rarefied appearance of the pleura is changed to a mottled or irregular condition, when a greater degree of collapse is noted without any further introduction of air, such a condition may be present.

COMPLICATIONS

The pulmonary complications of pulmonary tuberculosis are rarely revealed by physical signs but are usually diagnosed antemortem, if diagnosed at all, from the

roentgenogram. We refer to tumors arising in a tuberculous lung, bronchiectasis in a healing or healed tuberculous lung, localized atelectasis, and possibly bronchial stenosis. Pleural complications, often more readily accessible to physical examination, are frequently overlooked until discovered on roentgenologic study. Here we refer to the accessory lobes and their involvement, interlobar and mediastinal pleurisies, localized pneumothoraces. In the extrapulmonary complications the physical signs are frequently as useless, the roentgenogram often as helpful. Here we might mention intestinal tuberculosis, healed or healing tuberculosis of the spleen, and renal tuberculosis.

PNEUMONOCONIOSIS

We feel the day is not far distant when the diseases due to dust will be classified in stages more or less like those used in pulmonary tuberculosis, *e.g.*, slight, moderate, and advanced. The diagnosis, for example, of silicosis, so beautifully studied by Pancoast and Pendergrass, is on a much firmer basis to-day, as a result of their roentgenologic investigations. The various degrees of linear exaggeration and nodulation are slowly but surely being standardized, but to be able to say when pulmonary tuberculosis complicates the picture is another and more difficult matter. Physical signs are most often of slight value in the diagnosis of early silicosis, or, for that matter, when it is complicated with a minimal or moderately advanced tuberculosis. Here the roentgenogram is of the greatest value. Many cases approach death, in whom only the roentgenologic examination discloses the obvious disease. The two processes, *viz.*, silicosis and tuberculosis, have in the main characteristic shadows: (1) in silicosis, the nodulation, not unlike the pattern of miliary tuberculosis so familiar to everyone, and (2) the variegated pattern of tuberculosis in its many phases, also reasonably well recognized. If we superimpose—or, better, intermingle the one with the other—we have what is often seen and not infrequently proved to be tuberculo-silicosis or silico-tuberculosis. There appears to be little doubt that the burden of the diagnosis of pneumonoconiosis depends upon the roentgenologic study.

SUMMARY AND CONCLUSIONS

Recent advances in the study of the etiology, diagnosis, prognosis, prophylaxis, and treatment of pulmonary tuberculosis have been rather closely associated with technical improvement of the roentgenogram.

The roentgenogram should be used to perfect, not to replace, the usual methods of physical diagnosis in pulmonary disease.

The early lesions of childhood and adult pulmonary tuberculosis are detected sooner on the roentgenogram than by physical signs.

Only the roentgenogram yields data sufficiently accurate to be used in the classification of pulmonary tuberculosis. When a cavity is readily diagnosable by physical signs, the disease is usually in a far advanced stage. The great importance of cavity in the treatment of pulmonary tuberculosis makes its early diagnosis from the roentgenogram highly significant.

Serial roentgenograms are probably the most accurate means of determining activity. Prolonged experience enables some to estimate the presence of activity with fair accuracy from a single set of roentgenograms.

The roentgenogram is far more accurate than the physical signs in prognosis.

Collapse therapy, and especially thoracoplasty, have developed largely since the perfection of roentgenologic examination. Inference drawn from a study of physical signs is not sufficiently precise.

We wish to thank Dr. Heise for permission to publish many of the data in this article.

IRRADIATION THERAPY IN CANCER OF THE MOUTH: TECHNIC AND RESULTS[1]

By G. E. PFAHLER, M.D., Sc.D., *and* J. H. VASTINE, M.D., *Philadelphia*

CANCER of the mouth is now curable in the great majority of cases if treated early, thoroughly, and skillfully from the beginning by means of irradiation. While this represents a great advance, much is involved in carrying out the above requirements and, because they are not carried out, to-day only from 25 to 35 per cent of all cases recover. Early treatment means that patients must consult a competent physician when any sore, fissure, wart, or thickened white patch appears in the mouth and shows no tendency to heal within two weeks; otherwise, the best chances are lost. Early treatment further requires that a diagnosis must be made, or suspected, at the first visit by the physician, and immediate steps taken by him to obtain consultation or microscopic confirmation at the earliest possible moment. (It is our custom to give preliminary irradiation in all suspected cases, before doing a biopsy.) To meet these requirements it is further necessary to have sufficient radium and equipment available, and (and this is of the greatest importance) it is essential that a physician be available who is skilled in the application of the principles of radiology. The mere possession of radium is of no more consequence in itself than is the possession of a set of surgical instruments—it is the skill in their use which counts.

PRINCIPLES AND TECHNIC

It is not possible to prescribe a technic which will be adaptable to all cases of cancer of the mouth, since each case is a new problem which must be dealt with individually. The principles of the technic, however, can be fairly well standardized. These are based primarily upon the fundamental principles of radiation therapy, as follows: (1) Bérgonie and Tribondeau (1) found that cells are most radiosensitive during mitosis; (2) Dominici (13) found cells more radiosensitive the closer they approach the embryonic type; (3) Regaud and Lacassagne further investigated and proved the above principles and also found a greater differentiation in the sensitivity of the cancer cells as the wave lengths become shorter, represented by highly filtered gamma rays of radium. (We use from one to two millimeters of platinum, which is the equivalent of from two to four millimeters of lead.) In the application of these principles in the treatment of cancer of the mouth, early in 1924 we made use of larger quantities of radium (filtered at first through one millimeter of platinum and later through two millimeters of platinum), and prolonged the effect on the principles of the Saturation Method during a period of from three to four weeks, as reported (36) by one of us (G. E. P.) by invitation of the British Empire Cancer Campaign, before the International Conference on Cancer, held in London, in July, 1928. Since then this technic has been continued, and in certain cases we have supplemented this surface irradiation by interstitial irradiation as recommended by Regaud (43), Lacassagne (25), Quick (39), Martin (29), and others. We have made other reports since that date (35–38). Our results are improving progressively as our skill in the application of these principles has advanced, and consequently our optimism has increased.

Applications inside the Mouth.—We plan to give from 1,500 to 3,000 mg.-hrs. inside the mouth to the affected area within a period of from three to four weeks. Radium element is used filtered through 2 millimeters of platinum with sufficient rubber to make the distance 5 millimeters. Radium is applied in all

[1] Presented at the Eighteenth Annual Meeting of the Radiological Society of North America, at Atlantic City, Nov. 28–Dec. 2, 1932.

possible positions to obtain a cross-firing effect upon the primary lesion. Thus, in a lesion in the posterior portion of the tongue, radium is applied to the base of the tongue, to the dorsum of the tongue, side, on the tongue, and to the base of the tongue. This is at times supplemented by interstitial irradiation with platinum needles containing radium element.

Lesions about the *alveolus* are usually

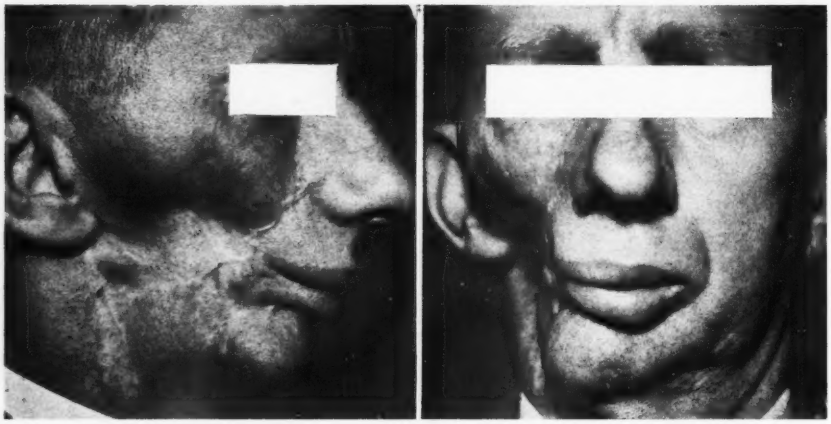


Fig. 1. Male, age 43, referred by Dr. L. H. Dick, Nov. 23, 1918. Epithelioma of right cheek developing during three years, due to tobacco-chewing. Disease destroyed by electrocoagulation, followed by osteomyelitis, and, later, resection of the lower jaw on the right side. Patient has been well for 14 years.

and in the floor of the mouth. Lesions in the anterior portion and margins of the tongue are treated by radium applications on the dorsum of the tongue and in the floor of the mouth. These surface applications are frequently supplemented by interstitial irradiation with platinum needles now containing 1, 2, or 3 milligrams of radium element and inserted preferably through the skin. If, as is frequently the case, lesions in the anterior or posterior portion of the tongue are of low grade malignancy, electrocoagulation, particularly of the smaller lesions, is performed as thoroughly as possible, together with the above irradiation. If the posterior portion is removed by electrocoagulation, the lingual or external carotid artery must be ligated. When electrocoagulation is performed the entire macroscopical disease must be removed.

In *sublingual lesions*, surface applications of radium are placed in the floor of the mouth on both the involved and opposite treated by surface applications only, since radium needles inserted into bone will produce an embarrassing necrosis. Radium is applied to the alveolus, in the gingivo-buccal fold, and in the floor of the mouth.

Lesions of the *cheek* are frequently of low grade malignancy, slow in developing, and relatively radioresistant. Therefore, we usually consider it desirable to introduce platinum needles containing small quantities of radium element, permitting them to act almost long enough to produce an escharotic effect. Radium is applied to the surface of the cheek, both inside and outside, also in the gingivo-buccal folds, in the posterior vestibule, and in the floor of the mouth.

Cancer of the *roof of the mouth* is irradiated by surface applications applied against the palate, inside of the nose, and outside of the alveolus.

The *tonsils* are irradiated by surface applications of radium applied on a tonsil

clamp, surface applications at the base of the tongue, in the posterior nares, and in the posterior vestibule. Needles containing radium element are at times used to supplement the above treatment, although some excellent results have been obtained by surface applications alone in the radiosensitive carcinomas usually occurring in the tonsil.

Cancers of the *mouth* vary in position, in extent, in duration, in amounts of fibrosis, and in radiosensitivity. In addition to the variations in the malignancy, there are variations in the host, both in his general health, his tolerance of and response to irradiation. Consequently, treatment of these lesions cannot be reduced to a general routine procedure—they must be individualized. Lead applicators of one-eighth inch in thickness, as described by Grier, can be cut and bent into any desired shape, permitting great accuracy in the placement of the radium and firmness in maintaining its position. Vulcanizing rubber, which adheres only to itself, has been used by one of us (G. E. P.) since 1918 in covering applications, its use being described in 1930 (38). Tonsil clamps are advantageous in applying radium to the tonsil, the region of the anterior pillar, or the lateral pharyngeal wall. Long curved tubes are convenient in holding the application against the pharynx, tonsil, or posterior surface of the tongue. Dental compound, as recommended by Ebling (15), is occasionally valuable in accurate fixation of the radium.

Irradiation must be given to the upper limit of normal tissue tolerance. With the highly filtered radium element, one is justified in producing an epithelitis of the mucous membranes of the mouth, with formation of a white membrane or desquamation over and about the lesion and along its paths of lymph drainage. Martin and Quimby and Pack (27, 42), in two excellent presentations, have described the lethal dose delivered to all parts of the tumor to be a minimum of from 3 to 11 skin erythema doses, usually from 8 to 11, depending upon the grade of malignancy. This has been a distinct advance, placing irradiation of cancers of the mouth on a more scientific basis, giving us something definite other than empiricism upon which to work. Nevertheless, we feel that every case of intra-oral malignancy should be treated to the very limit of normal tissue tolerance.

Electrocoagulation is used in conjunction with irradiation in cases in which the lesion is small and of low grade malignancy; in lesions developing on a leukoplakia (it being best to destroy the leukoplakia so far as possible in order to prevent the future development of new lesions), and in recurrent lesions which have been previously irradiated, with the resulting presence of considerable fibrous tissue. The general damage to the mucous membrane in cases of leukoplakia renders new lesions liable in other parts of the mouth.

External irradiation is of the greatest importance to control the metastases. Irradiation is routinely given over the regional areas of lymph drainage, constituting the lower face, submaxillary and submental regions, and the entire neck in cases of intra-oral malignancy. Simmons (51) found histologic evidence of *metastatic malignancy in 34 per cent* of his series of intra-oral cancers in which there were no *palpable lumph nodes*. This is too high a percentage to permit of only local treatment of the primary lesion, even when no lymph nodes are palpable.

External irradiation is applied by means of radium element filtered through at least 3 millimeters of brass, but, better, through 2 millimeters of platinum or its equivalent at a distance of four or five centimeters, a total of from 30,000 to 60,000 mg.-hrs. being given in from 3 to 4 weeks. This is applied on molds of Columbia paste (Esquerra, Monod, and Richard, 16) or felt packs or sponge rubber, on both sides of the face and neck. In addition, capsules or radium element filtered through 2 millimeters of platinum are sometimes placed in rolls over a node to obtain a more intense local effect. Inter-

stitial irradiation is used in the treatment of definitely palpable nodes, being given by needles containing 5 or 10 milligrams of radium element filtered through 0.4 millimeter of platinum, introduced in and about the nodes by puncture of the skin. inserted interstitially and permitted to remain for from five to seven days, the number of needles used depending largely upon the extent of the disease, and the time depending largely upon the amount of surface irradiation which is planned.

Fig. 2. Male, age 65, referred by Dr. G. H. Seiberling, April 6, 1927. Tumor filling the entire inside of the right cheek, mandible involved, and growing during seven years, worse during the last year. Section by Dr. Eugene Case showed squamous-cell carcinoma, Type 1. Responded rapidly to radium; no recurrence during five years.

Regaud has recommended interstitial irradiation in needles containing a small amount of radium element. These smaller quantities of radium are left in the tissues for from seven to fourteen days, depending upon the factors employed, thus obtaining continuous irradiation over a long enough period to affect all cells during their period of mitosis. These principles are the basis of treatment at the Curie Institute at the present time, while Cade (8, 9), Birkett (4, 5), Gask (22), Martin and Sharp (28), and others have reported success in the use of this type of irradiation. We have employed needles containing 1 milligram of radium element in needles 2.8 centimeters in length, 2 milligrams of radium in needles 4.4 centimeters in length, and 3 milligrams of radium element in needles 6 centimeters in length, the filtration being 0.5 mm. of platinum for the first two, and 0.6 mm. for the 6 cm. needles. A total of from 30 to 50 milligrams is

There have been 11 cases in which there was definite, extensive involvement of the lymphatic glands. It is too soon to permit definite conclusions, but the fact that 6 (or 54.5 per cent) of these are apparently well for periods of from sixteen to twenty-one months is definitely encouraging. These results have been obtained in advanced, inoperable, apparently hopeless cases.

Cancer of the tongue is the most frequent, most serious, and most rapidly developing cancer of the mouth, constituting 47 per cent in our series. Of these, 53 per cent belonged to the third and fourth grades of malignancy. Broders (6) classed a little more than half and Berven, 47 per cent of the epitheliomas of the tongue as belonging to Grade 3. Cancer of the tongue metastasizes early and rapidly; therefore, the treatment of all cancers of the tongue and, generally speaking, all cancers of the mouth become a radiological problem.

Lane-Claypon (26), in 1930, from an extensive and comprehensive analysis of the literature regarding cancer of the tongue from a statistical standpoint, concluded that the cases treated radiologically show a more favorable survival rate after three years than those treated surgically. In 1930, Regaud reported on 344 cases treated at the Curie Institute, with 24 per cent cures during from one to seven years, but of these 344 cases only 20 per cent were in the operable stage. Berven (2, 3), in 1927, and again in 1931, reported on 104 cases of cancer of the tongue, with a recovery of 32 per cent of all cases, both early and advanced, and free from disease after five years, while 59 per cent of the early cases were symptom-free after three years. Quick (40), in 1929, reported on 450 cases of carcinoma of the tongue treated by irradiation, with 22.4 per cent recovery, but 50 per cent of these had been advanced and inoperable.

Cade (9), in 1930, reported on 169 cases of lingual carcinoma of which 47.9 per cent were alive and free from evidence of disease. The majority of these cases were of less than two years' duration and the passage of additional time is necessary to permit of definite conclusion. Cade favors the employment of long needles containing small amounts of radium element, with high filtration. These are introduced about the primary lesion and are left in the tissue for from seven to ten days. The cervical region is irradiated routinely with surface applications of radium on packs. Small glands are dissected out, while large glands are treated by interstitial irradiation with radium element needles.

Birkett (4), in 1930, reported on 267 cases, with from 22.5 to 45.1 per cent of the patients alive and well four to two years, respectively. He favors the employment of radium element in needles used interstitially about the primary lesion, with no further treatment if there are no palpable metastases. If nodes are palpable, block dissection is performed, followed by insertion of long needles containing small amounts of radium element. These are left in the tissues for eight days.

Schreiner and Brown (48), in 1925, reported on 127 cases of carcinoma of the tongue, with 34 per cent clinically well for periods up to four years. Palliation only was obtained in those cases with metastases.

Soiland and Meland (54), Roux, Berger, and Monod (47), Simpson and Flesher (52), Fitzwilliams (20), Fischell (19), Scott (50), Smith (53), Stewart (55), Widmann (56), Martin and Sharp (28), have made valuable contributions. Grier's method (23, 24) of making local surface application with lead adapted to the individual needs has been a definite advance in technic.

Our Results.—Of 186 cases of carcinoma of the tongue treated since 1904, 172 could be traced, of which 62 (36.1 per cent) are living and free from evidence of disease. Excluding the cases which could not be traced, 32.4 per cent of the patients were living and well three years after treatment, and, counting the untraced cases as dead, we have an absolute three-year curability of 29.3 per cent. This includes 89 cases with palpable nodes, of which 17.8 per cent have been well for periods varying from one and one-half to nine years. Some of these palpable nodes were probably inflammatory, as Simmons has shown that 46 per cent of the palpable nodes which were dissected out by him proved to be. Nevertheless, this represents a group in which surgeons report cures in only from 3.8 to 17 per cent, and the surgical series probably do not include the number of advanced cases included in this series, for it is doubtful whether any surgeon would have the temerity to operate on many of the patients in our series. Of the 97 patients without palpable nodes, 37.1 per cent were symptom-free three years and more after treatment. Of the 70 patients treated since 1925 by the technic now in use, 31.4 per cent have been well for periods of from one to six years after treatment.

We must always assume that there is metastasis present, as has been shown by

TABLE I.—RESULTS IN 396 UNSELECTED CASES OF CARCINOMA OF THE MOUTH TREATED SINCE 1904, WITH VARIOUS TYPES OF TECHNIC

	Cases	Cases traced	Alive	Percentage alive	Dead	Percentage dead
Tongue and floor of mouth	186	172	62	36.1	110	63.9
Cheek	68	65	33	51	32	49
Tonsil	31	26	7	27	19	73
Lower jaw	50	46	14	30.5	32	69.5
Upper jaw and roof of mouth	61	55	23	41.8	32	58.2
Total	396	364	139	38.2	225	61.8

		Alive				
	Av. dur. (mos.)	Less than 1 yr.	1–3 yrs.	3–5 yrs.	Over 5 yrs.	Average
Tongue and floor of mouth	10.9	4	12	11	35	7.1 yrs.
Cheek	19	3	9	7	14	5.4 yrs.
Tonsil	24	2	2		3	6.6 yrs.
Lower jaw	7	2	2	4	6	5.4 yrs.
Upper jaw and roof of mouth	4.8	3	5	4	11	5.2 yrs.
Total	13.1	14	30	26	69	6.1 yrs.

	3-yr. recoveries (traced cases) %	Recovery (all cases) %
Tongue and floor of mouth	32.4	29.3
Cheek	42.9	40.3
Tonsil	13.6	11.1
Lower jaw	27.7	25
Upper jaw and roof of mouth	34.1	30
Total	32.4	29.3

TABLE II.—RESULTS BY PRESENT TECHNIC IN UNSELECTED CASES OF CARCINOMA OF THE MOUTH, BOTH EARLY AND ADVANCED[2]

	No. cases	Well		Duration
Tongue and floor of mouth	70	22	(31.4%)	1–6 yrs.
Cheek	34	20	(58.8%)	1–7 yrs.
Tonsil	15	4	(26.6%)	6 mos.–3 yrs.
Lower jaw	27	9	(33.3%)	1–7 yrs.
Upper jaw and roof of mouth	25	12	(48.0%)	1–7 yrs.
Total	171	67	(39.2%)	

Cases with Palpable Lymph Nodes

	No. cases	Recoveries	
Tongue and floor of mouth	89	16	
Cheek	19	7	
Tonsil	19	4	
Lower jaw	20	6	
Upper jaw and roof of mouth	10	4	
Total	157	37	(23.5%)

block dissections when no glands were palpable (34 per cent of the cases reported by Simmons, 51). Of the cases with clinically palpable neck nodes operated upon by DeVecchi (12), 57 per cent showed histological evidence of malignancy.

It is our custom to use from 30,000 to 60,000 milligram-hours of irradiation externally, with from 20 to 30 ten-milligram units distributed over the lymphatic drainage areas and applied at intervals during a period of from three to four weeks, filtered through the equivalent of from 3 to 4 mm. of lead, and at a distance of from 4 to 5 centimeters. This should cause a deep redness, and desquamation of the skin. It is further supplemented by surface application inside the mouth, and fre-

[2] These cases are taken from the records in Dr. Pfahler's private office (where 1,250 milligrams of radium are in use).

quently interstitial irradiation. We believe, when possible to reach the disease, this interstitial irradiation is best applied through the skin, in small quantities, filtered through 0.5 mm. of platinum, and

Fig. 3. Female, age 69, referred by Dr. Frank R. Sheppard, Jan. 10, 1922. Duration, six months. Squamous-cell epithelioma involving entire roof of the mouth and right cheek; treated by radium and finally electrocoagulation in the right cheek; no recurrence during five years. Patient died of myocarditis in November, 1927.

allowed to work for from four to seven days.

Cheek.—Carcinoma of the cheek constituted 17.1 per cent of the intra-oral malignancies of our series. Fraser (21) reports carcinoma of the buccal cavity to be eight times as frequent in males as in females, probably because of irritation due to the use of spirits and tobacco. These figures are reversed for the population of southern India and Ceylon where the women chew betel (a combination of tobacco, areca nut, and slacked lime).

Malignancy.—Lesions arising from the inside of the cheek are usually less malignant than those arising from the tonsil and tongue. Thus, 82 per cent of the lesions which were graded histologically belonged to Groups 1 and 2. Broders classed 62 per cent of cases of epithelioma of the cheek in Grades 1 and 2. Birkett states that carcinomas of the cheek are comparatively of high differentiation. Despite the fact that the grading of tumors histologically is practised at the Mayo Clinic, the New York Memorial Hospital, Huntington Memorial Hospital, Radiumhemmet, Curie Institute, St. Bartholomew's Hospital and many other equally renowned clinics, it is not universally accepted as of value, since, at times, different sections from the same tumor show all different grades of malignancy. The lower degree of malignancy of these lesions histologically closely corresponds to the clinical manifestations. Thus, the average duration of lesions of the cheek was 19 months before coming for treatment. This was very much longer than in any other site in the mouth, except in the region of the tonsil, indicating that the lesions were usually slow-growing. The average duration of the lesions in the tonsil cases was greater, due to several post-operative recurrences after a number of years, increasing the average duration to such an extent that it is not representative. It is also likely that these patients had a chronic tonsillitis before the malignant disease, which increases the duration of symptoms. This has a definite practical

value bearing upon treatment as discussed under "Technic."

Results of Radiological Treatment.—Berven, in 81 cases of carcinoma of the inside of the *cheek*, reported 26 per cent of the cases symptom-free five years after treatment. *Our results of 68 cases of carcinoma of the cheek* show that 65 could be traced, of which 33 (51 per cent) are living and free from evidence of disease. Excluding the three cases which could not be traced, 42.9 per cent of the patients were living and well three years after treatment, and, counting the untraced cases as dead, we have an absolute three-year curability of 40.3 per cent. This includes 19 cases with palpable lymph nodes, of which seven (36.9 per cent) have been living and well for periods of from two and one-half to nine years. Five (26.3 per cent) of these cases are well three years or more after treatment. Four patients with bone involvement are all dead. Of the patients without palpable lymph nodes, 34.8 per cent are well three or more years after treatment. Of the 34 patients treated since 1925 by the newer technic, 20 (58.8 per cent) are well.

Tonsil.—Malignant tumors of the tonsil are comparatively rare, representing only 7.8 per cent of all of the intra-oral malignancies in our series of cases. Pack and LeFevre report 9.6 per cent of their intra-oral tumors as arising from the tonsil and further report malignancies of the tonsil as constituting 2.23 per cent of a series of 16,555 unselected cases of malignant tumors admitted to the Memorial Hospital. Of *our series* of 31 cases of malignancy of the tonsil 9.7 per cent were sarcoma; thus the incidence of carcinoma was about ten times as great as sarcoma. New and Childsey (31) reported 14.5 per cent and Duffy (14) reported 8.6 per cent of malignancies of the tonsil to be lymphosarcoma.

While we feel strongly that irradiation is the treatment of choice in all cancers of the mouth, we are convinced that, due to certain factors, this is particularly true of malignancies of the tonsil. These factors follow.

(1) *High Degree of Malignancy of These Tonsil Tumors.*—The great majority (87.5 per cent of those classified) in our series being Grade 3 or 4 epithelioma (Broders classification), transitional-cell epithelioma or lymphosarcoma, this statement must be made by us with reservations since the microscopic examinations were made by numerous pathologists, the biopsy frequently having been taken elsewhere before the patient was referred for irradiation. Broders (6), from a series of tonsil cases at the Mayo Clinic, reported 94.1 per cent as belonging to Grades 3 and 4. Berven reported 93 per cent of carcinomas of the tonsil as belonging to Grades 3 and 4. We are not qualified as clinicians to discuss the merits of tumor-grading or the pathologic characteristics of transitional-cell epithelioma of Ewing, and lympho-epithelioma of Regaud and Schmincke. We do believe, however, that the majority of tonsillar neoplasms are of a high degree of malignancy and are consequently radiosensitive.

(2) *Early Metastasis from Malignancies of the Tonsil and Consequent Hopelessness of Any Other Method of Treatment Other Than Irradiation.*—It not infrequently occurs that metastatic cervical nodes are the first evidence of malignancy, the primary lesion in the tonsil being so small as to have escaped attention. Of our series, 61 per cent had definitely palpable lymph nodes when they came for treatment. This compares closely to the findings of New and Childsey, 65 per cent of their cases having metastatis in the cervical lymph nodes at the time of admission. Duffy reported 58.2 per cent as having palpable lymph nodes when treatment was begun.

(3) *Relative Inoperability of Tonsillar Malignancies.*—This is due to the usually high degree of malignancy, with early metastasis and the technical difficulties encountered in removal of tonsillar malignancy. This fact is attested to by the dearth of reports on series of cases treated

surgically. Thus, as Burnam (7) states, since the Matthews report, in 1912, of the surgical results obtained in treating malignant tumors of the tonsil, there are no satisfactory reports of extensive series of

Fig. 4. Male, age 60, referred by Dr. A. S. Knight, Oct. 11, 1922. Wassermann negative. Carcinoma of the tongue, with metastasis. Duration, six weeks. Treated by radium; well over ten years to date.

cases from a single clinic, although there are numerous individual cases reported in the literature. *Berven states that surgical treatment is scarcely able to show a single case of healing. There have been no surgical cures of carcinoma of the tonsil at the Radiumhemmet.*

In contrast to this dearth of literature upon the surgical treatment of neoplasms of the tonsil, during recent years there have been comprehensive reports on *irradiation treatment* of these relatively uncommon malignancies. These reports have been by men of the highest caliber on rather extensive series of cases. Thus, Berven, in 1931, reported on 89 cases of malignancy of the tonsil. He reports a 39 per cent three-year cure of the cases of carcinoma treated by their recent technic (teleradium externally and surface radium applications to the tonsil and implantation of radium needles or endothermic removal of small residual lesions). He reports a 43 per cent three-year and 38 per cent five-year healing in 35 cases of sarcoma of the tonsil. Burnam (7), in 1931, reported on 133 malignancies of the tonsil treated by irradiation, with a 4.12 per cent cure in carcinoma and a 20 per cent cure in sarcoma. This, however, includes many cases not traced and counted as dead, many cases treated by older methods, and many very advanced hopeless cases. Of his cases treated in 1929 and 1930, 50 per cent are well and free from any evidence of disease. These cases were treated by a more recent technic consisting of teleradiation externally and interstitial irradiation with radon needles. Coutard, in 1931, reported on 46 *advanced* cases of carcinoma of the tonsil treated by roentgentherapy alone, with five-year cures of 23 per cent. These were all extensive lesions, but, *in the Curie Institute, epitheliomas of the tonsillar region even of limited extension, are treated preferably by radium therapy.*

In 1931, New, Broders, and Childsey (32), reporting on 45 cases of lymphosarcoma and Types 3 and 4 carcinoma of the tonsil, write that 55 per cent of the cases of lymphosarcoma were alive for an average of almost seven years, and 36 per

cent of the cases of carcinoma, Grades 3 and 4, were alive for an average of almost four years. They treat cases of low-grade malignancy by removal by surgical or diathermic measures, followed immediately by introduction of radium needles or radon into the wound. They state that if the lesion is extensive, with or without large lymph nodes, irradiation probably offers the only chance. They advise irradiation alone as the indicated treatment in lymphosarcoma.

Duffy (14), in 1923, reported on 122 cases, 49 of which were for a period of over five years in which group there were 10 (20.4 per cent) free of disease. He subjects the neck to both x-radiation and radium packs externally, combined with interstitial irradiation with radon implants locally to the primary lesion. Robinson (46), in 1929, reported on 27 epidermoid carcinomas, with 18.5 per cent well two or more years after treatment. He used interstitial irradiation in treating the primary growth and radium packs externally. Schreiner and Simpson (49), in 1929, reported 17 of the patients without palpable metastasis as well for five years and 4 per cent with palpable metastasis well for five years.

Our results on 31 cases of malignancy of the tonsil treated since 1904, show that 26 could be traced of which 7 (27 per cent) are living and free from evidence of disease. This represents a three-year curability of 13.6 per cent excluding the five cases which could not be traced, or an absolute three-year curability of 11.1 per cent counting the untraced cases as dead. This at first glance would not seem encouraging but we do not believe this represents the curability of these malignancies employing more recent technic. It is interesting to note that four, or *26.6 per cent of the cases treated since 1925*, are alive and free from evidence of disease. While all of these cases are not five years in duration, we feel that the results are encouraging and warrant further employment of our present technic. Carcinoma of the lower jaw constituted 12.6 per cent of our series of cases of intra-oral malignancy.

As to the malignancy of those cases which were graded histologically, 45 per cent were Type 3, the remainder being divided between the three remaining groups. Broders classifies epithelioma of the gums with epithelioma of the lips, in which group 62 per cent belonged to Grades 1 and 2. It can be seen that lesions in this region are of a lower degree of malignancy and, according to Martin, Quimby, and Pack (27, 42), would require greater amounts of irradiation in the tumor than in lesions of the tongue, palate, and tonsil, the latter being usually more anaplastic and consequently more radiosensitive.

Results of Radiological Treatment.—Of 50 cases of carcinoma of the lower alveolus, 46 could be traced, of which 14 (30.5 per cent) are well. Excluding the four cases which could not be traced, 27.7 per cent of the patients are well three years after treatment, while counting the untraced cases as dead, we have an absolute three-year curability of 25 per cent. This includes 20 cases in which there were palpable nodes, of which 6 (30 per cent) have been well for periods varying over one year. Of 11 cases in which there was bone involvement, 4 (36.3 per cent) have been well for two, two and one-half, five, and seven years, respectively. Of 27 cases treated since 1925 by the newer technic, 33.3 per cent are well. Berven reported 24 per cent of 34 patients treated by the newer technic as free from signs and symptoms of cancer five years after treatment. This technic corresponds closely to that employed by us.

Upper Jaw and Roof of Mouth.—Carcinoma of the upper jaw and roof of the mouth constituted 15.4 per cent of our series of cases of intra-oral cancer. Chemin (10) reported carcinoma of the gums and palate as constituting 1.1 per cent of all tumors seen. The malignancy of those cases was graded histologically, 72 per cent belonging to Grades 1 and 2. Lesions of the alveolus are usually of a lower degree

of malignancy. Epithelioma of the palate is usually of a higher grade of malignancy than lesions of the alveolus. Thus, Broders, in a group of carcinomas arising from the hard and soft palate and the pharynx, found 47.05 per cent to belong to Grade 2; 35.29 per cent to Grade 3, and 17.64 per cent to Grade 4. The group containing lesions from the upper jaw consisted of 7.60 per cent Grade 1, 54.38 per cent Grade 2, 34.5 per cent Grade 3, and 3.5 per cent Grade 4.

Results of Radiologic Treatment.—Of 61 cases of malignancy of the upper jaw and palate, 55 of our cases could be traced, of which 23 (41.8 per cent) are well. Excluding the cases which could not be traced, there were 34.1 per cent of the patients living and free from evidence of disease three years or more, or an absolute curability of 30 per cent counting the five untraced cases as dead. Of the 25 cases treated by the improved technic, 48 per cent have been well for periods varying from one to eight years. There were 10 cases in which there were definitely palpable lymph nodes, of which four are well from two and one-half to seven years later. There were 19 cases in which there was bone involvement; of these, seven are living for periods of from six months to nine years.

Berven (3) reports 18 per cent of the patients with carcinoma of the upper jaw symptom-free four years or more after radiologic treatment; Quick reports 22 per cent well for periods of from six to thirty-nine months; Johnson reports 20 per cent well for periods of from one to five years; Schreiner reports 10 per cent well for periods of from one to nine years.

SUMMARY AND CONCLUSIONS

1. This report is based upon 396 unselected cases of cancer of the mouth (not including lip cases) treated by various forms of irradiation technic during its evolutionary stages, since 1904, but chiefly since 1920, with a recovery of 29.3 per cent.

2. Of the 171 cases treated by our present technic, there has been recovery in 39.2 per cent.

3. The low percentage of recoveries is due to the delays and incomplete treatment in many of these cases when they first consulted a physician.

4. We believe that from 50 to 75 per cent of mouth cancers should get well if patients can receive thorough and skillful treatment by irradiation from the beginning.

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THE ROENTGEN DIAGNOSIS OF ATELECTASIS

WITH SPECIAL REFERENCE TO THE GROUND-GLASS SHADOW AND THE DEGREE OF PULMONARY SHRINKAGE

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ATELECTASIS is not diagnosed with entire satisfaction by means of the x-ray, owing partly to a lack of unanimity as to the definition of the term, and partly to a lack of pathognomonic signs.

The situation regarding the first cause is as follows. Standard text-books of pathology refer to atelectasis as a totally airless state of the entire lungs, or of any part of them, with collapse of the small airways and alveoli (the walls of these compartments lying in direct contact with one another, 1). This refers alike to the three recognized types of the disease—congenital, obstructive, and compressive. Most clinical writers have adhered to these criteria, but recently some have extended the meaning of the term to include nearly all conditions in which it is evident from examination of the living subject that the lung is denser than normal and reduced in size, regardless of the nature of the consolidation. For instance, Coryllos and Birnbaum (2) call pneumococcal pneumonia and atelectasis one and the same disease, mainly because, in both, the lung is consolidated and smaller than normal. Coryllos (3) illustrates the histologic appearances of atelectasis with photomicrographs of lungs in which the alveoli are filled with inflammatory exudate (pneumonia). Some authors include under atelectasis a variety of states in which the pulmonary tissues are partially air-containing and lack complete alveolar collapse in any part. An extreme example of this is the condition of the lower lobes of the lungs in post-operative elevation of the diaphragm—that situation which follows most abdominal operations and in which the diaphragm stands nearly motionless at about the position of normal complete expiration. Other examples are the semi-inflated states of the lungs which exist in conjunction with deformities of the thoracic walls, with intrathoracic tumors, or with partial pneumo- or hydrothorax.

Such relationship as exists between pneumonia and atelectasis does not at all warrant merging them. True enough, patches of obstructive atelectasis commonly develop as pneumonia advances (4) because masses of viscid exudate collect in the bronchi of the inflamed part, metastasize, and plug the bronchi of neighboring parts. Also, it is now generally believed that areas of obstructive atelectasis contaminated with pneumococci are more prone to develop pneumonia than are areas of normally inflated lung so contaminated. However, both experimental and clinical experience have indicated that neither disease constantly precedes the other and that these diseases do not always accompany each other. Thus, the classical work of Blake and Cecil (5) on the pathogenesis of pneumonia demonstrates that pneumococci enter the lungs by way of the peribronchial lymphatics and travel by those paths to the periphery, so that the alveoli, not the bronchi as Coryllos contends, are the first of the airways to be involved with inflammatory exudate. The clinical pathologist has frequent opportunity to examine the lungs in the extremely early stages of pneumonia, but he does not regularly, or even usually, find atelectasis (Figs. 9 and 10).

It is equally unwarranted to class

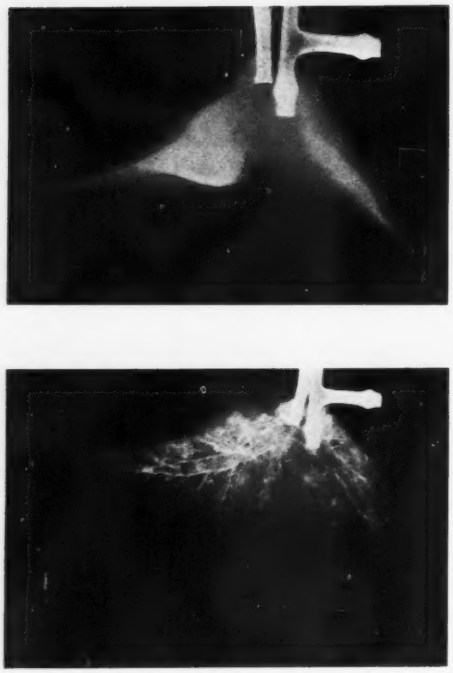

Fig. 1. (*Above*): Massive atelectasis of one entire lobe of a dog's lungs, showing the ground-glass-like appearance of the roentgen shadow. The atelectasis was produced by bronchial obstruction during the last 24 hours of life. (*Below*): Same lobe, after inflation to about normal size, demonstrating the increased radiolucence and size and the finely traced structural markings.

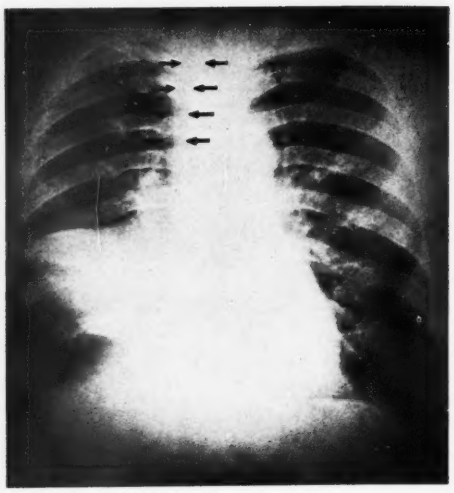

Fig. 2. Massive atelectasis of the entire right middle lobe (male, 67 years) due to obstruction of the corresponding lobar bronchus by carcinoma. The shadow of the lobe exhibits the ground-glass sign and an extreme gradation of density. The right hemidiaphragm is lifted and the heart and trachea are attracted toward the lesion.

partially air-containing states of the lungs with atelectasis. If the pulmonary condition in uncomplicated post-operative elevation of the diaphragm is termed atelectasis, then it must be said that all persons develop the latter disease with every maximum expiration! These semi-expanded states of the lungs are more reasonably referred to by Overholt's (6) expression, namely, "pulmonary hypoventilation," since the affected parts carry on a definite, though reduced, respiratory exchange with the outer atmosphere, while atelectatic tissues are totally without external respiration.[1] The distinction between hypoventilated and atelectatic lungs is not only theoretically sound but also of practical significance; for it differentiates between the pulmonary states of partial work and complete rest, which may be clinically important, especially in the therapy of pulmonary tuberculosis with artificial pneumothorax.

The lack of pathognomonic signs in the diagnosis of atelectasis and the mistakes which arise therefrom will be evident from the following brief survey of the roentgen diagnosis.

The most characteristic roentgenographic feature of unilateral, obstructive, or congenital atelectasis is ordinarily taken to be the gross reduction in the size of the affected tissues that is indicated by certain displacements of the pulmonary environs—the half of the diaphragm on the side occupied by the lesion is elevated, and a part or all of the mediastinum is carried toward that side. Both of these displacements appear with lesions involving comparatively small parts of the lung as well as with those extending over large portions.

[1] These partially air-containing states of the lungs may remain without change for long periods; whereas, according to many observers, any part of the lungs that is cut off from all external exchange of air for more than a few hours becomes *completely* airless.

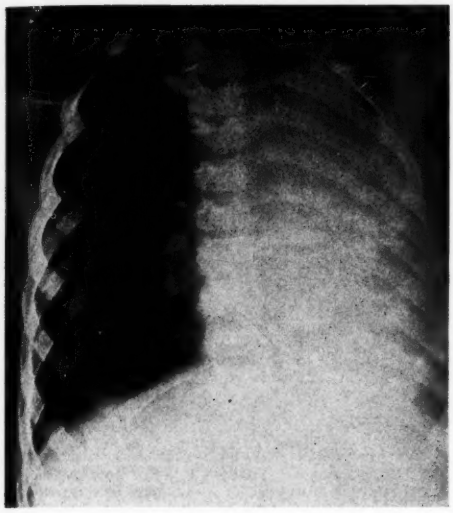

Fig. 3. Massive atelectasis of the whole left lung (male, 6 years) developing from obstruction of the left primary bronchus by a plug of mucus, five days after the onset of bronchopneumonia of the left lower lobe. The ground-glass shadow is presented in the intercostal spaces of the entire left lung-field, although it is most easily recognized at the periphery. The heart is missing from its normal position and lost in the shadow of the left lung-field. The left hemidiaphragm is also indistinguishable. The intercostal spaces on the side of the lesion are narrowed and the spine is slightly bent.

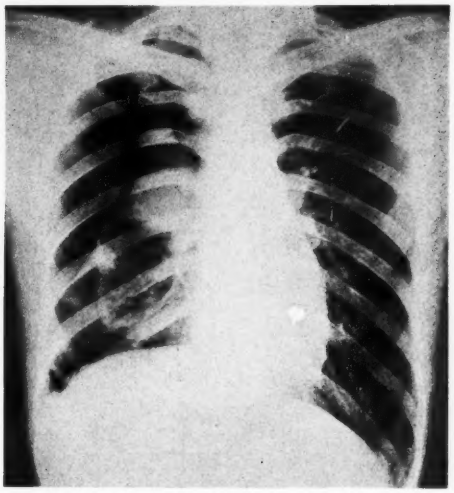

Fig. 4. Massive atelectasis of a tuberculous right upper lobe (male, 36 years) caused by artificial pneumothorax. The lobe was adherent at the apex so that it was compressed only from the sides. Its light ground-glass-like shadow contrasts with the mottled shadows of the partially collapsed, hypoventilated lobes below. The right hemidiaphragm is elevated but the mediastinum is not displaced.

When the atelectasis is confined to the lower lung-field, the heart may be the only mediastinal organ showing distraction; when the lesion is limited to the upper field, the trachea alone is often displaced, and when the entire hemilung is involved, both organs are displaced. The bony parts of the chest give the least evidence of dislocation: the ribs on the side with the atelectasis are commonly drawn somewhat together and downward, while those on the opposite side are spread apart and elevated a little more than normal. The spine sometimes becomes slightly scoliotic, with the concavity of the curve directed toward the lesion. The respiratory movements are changed; the hemidiaphragm and ribs on the side of the lesion move less than normally, while those on the other side usually compensate by moving more than normally. The mediastinum has a pendulum-like swing, with motion toward the side of the lesion at inspiration and away from it at expiration.

Bilaterally symmetrical, obstructive, or congenital, atelectasis shows no mediastinal displacements nor inequalities in position and movement of the diaphragm and ribs on the two sides. This is also true of compressive atelectasis, where the diaphragm, mediastinum, and ribs are either unchanged in position or are displaced in directions opposite to those that have just been described.

These features of atelectasis are quite generally recognized and agreed upon, but unanimity is lacking as regards the nature of the shadow cast by the pulmonary tissues themselves. Some observers (7, 8) find the shadow homogeneous, others (9), mottled or streaked, and many more, without constant composition; again some find the shadow only slightly more radiopaque than the normal lung, and others (9, 10), so very opaque as to be indistinguishable from the shadows of the heart, liver, and ribs with

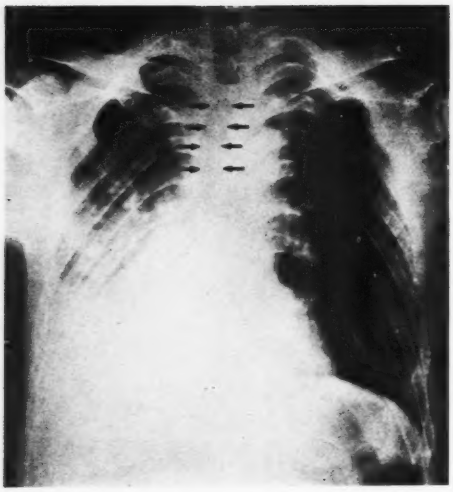

Fig. 5. Focal obstructive atelectasis of the lower part of the right lung (male, 53 years) which developed 24 hours after cholecystectomy. The affected part is denser than normal throughout and presents mottlings, but there is no ground-glass appearance. The heart and trachea are drawn toward the lesion. The right hemidiaphragm is indistinguishable.

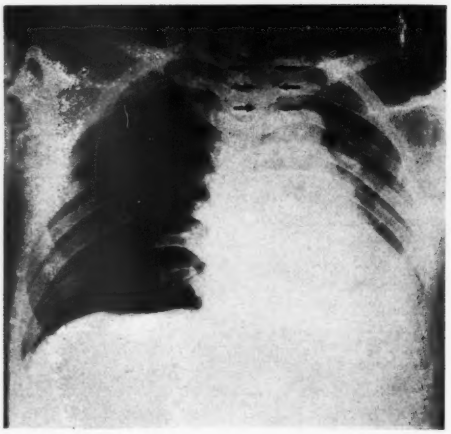

Fig. 6. Focal obstructive atelectasis of the whole left lung (male, 27 years) which formed two days after appendectomy. The left lung-field is dense and mottled but without the ground-glass sign. The mediastinum is displaced toward it. The position of the left hemidiaphragm is hidden.

which it merges. It has been discovered that the lung is most dense in postoperative atelectasis and least so in the compressive form of the lesion (7), the explanation given for this being that greater amounts of interstitial inflammatory fluids are usually present in the lung in the former condition (11, 12). As far as we can find, no writer in stating that the shadow may be either homogeneous or heterogeneous suggests a cause; nor has any one called attention to the use that can be made of the composition of the pulmonary shadow as a means of differentiating types of atelectasis or of distinguishing atelectasis from other diseases which produce increased density of the lung.

All these signs may occur in certain other pulmonary diseases. Many (13–18) have found them in pneumonia and have called attention to the uncertainty of diagnosis arising on that account. Wu (18) found definite diaphragmatic elevation in 55 per cent of cases of pneumonia and mediastinal dislocation in 12 per cent. Manges (19) and Packard (20) point to the circumstance that the lung markings and environmental displacements which characterize obstructive atelectasis may appear also in fibroid pulmonary tuberculosis, and they believe that mistakes in diagnosis are often made on that account.

This insufficiency in diagnosis led us three years ago to begin seeking systematically for new roentgen signs to distinguish between atelectasis and other lesions which produce consolidation of the lung-fields. It seemed possible that a roentgenographic study of the naked lungs might disclose differences in the consistency of the shadow of these lesions which, when specially looked for, could be detected easily in clinical thoracic roentgenograms. Accordingly the study was undertaken. Also, some information as to the size relationships of diseased and normal lungs, which was obtained from experiments of Van Allen, Wu, and Wang, seemed applicable to the differential diagnosis of atelectasis, and this matter was tested. A terminology of atelectasis was employed which was compatible with both

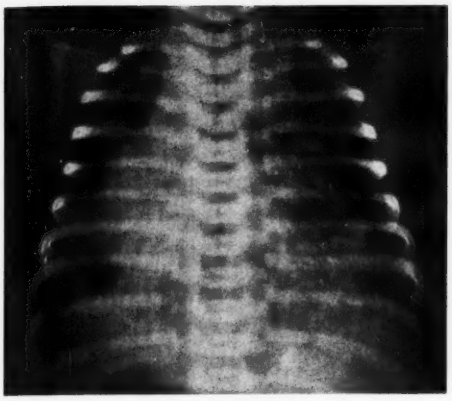

Fig. 7. Focal congenital atelectasis of both lungs (female, 3 hours). The child was markedly dyspneic and cyanotic at the time. Both lung-fields show mottlings which are roughly arranged in lines radiating from the hiluses, but no ground-glass sign.

Fig. 8. Congenital atelectasis in the lungs taken from a still-born infant. *Above:* the left lung, showing the ground-glass appearance of massive atelectasis. *Below:* the right lung after partial artificial inflation, giving the mottled shadow of focal atelectasis, with a radial arrangement somewhat similar to that in Figure 7.

the pathology of the disease and the clinical requirements.

Terms.—"Atelectasis" was used in the restricted sense to mean that state of the lungs as a whole or in any part with complete airlessness and alveolar collapse. It was referred to as *massive* when the area involved was large enough to permit the consistency of its roentgen shadow to be determined, and as *focal* when the area was not so large. (This brought under focal atelectasis, not only the single and isolated areas of alveolar collapse, but also the varieties in which the areas of collapse are minute, multiple, and more or less widely distributed.)[2]

Method of Study of the Pulmonary Roentgen Shadow.—Material of three types was secured and analyzed: First, massive atelectasis was produced in several dogs by plugging a lobar bronchus for 24 hours. The animals were sacrificed, the lungs removed, and roentgenograms made of both the normal and the atelectatic lobes. The atelectatic lobes were reinflated artificially and roentgenographed again. Second, specimens of human lungs, which *in toto* presented examples of the three types of atelectasis and of all of the common consolidating lesions of other varieties, were obtained fresh at autopsy, roentgenograms were made of them, and the nature of the lesions was checked by gross and histologic examination. Third, roentgenograms of the chests of living human subjects presenting these lesions, of which the diagnosis was made as accurately as possible by all known clinical methods, were collected. The lung shadows in the three

[2] The adjectives, lobar and lobular, are commonly employed by others to denote the forms of distribution of atelectasis, but they are anatomical terms used properly only by the pathologist. The clinical roentgenologist is seldom in a position to know with certainty the boundaries of the lesion relative to these units of structure. Thus, autopsy has often shown that lesions thought clinically to be lobar actually involved a little less or a little more than one lobe (Fig. 17). Indeed, the roentgenologist does not need to define the boundaries of the lesions so accurately. The terms *focal* and *massive* have been used before, of course. They have no reference to anatomical units but when the expression "of the upper (or middle or lower) lung field, anterior (or posterior) part" is added, they indicate well enough the distribution of the lesion. Their chief advantage lies in the fact that, when used in conjunction with the diagnostic signs to be described, they differentiate two clinically distinct varieties of atelectasis in each of the three recognized types of the disease. This will be evident from what follows.

Fig. 9. Extremely early bronchopneumonia and congestion in the right upper pulmonary lobe taken from an adult human being after death and inflated to about normal size. The left lower quadrant of the specimen presents the mottlings of the lesions, while the other parts show the delicate tracery of normal lung structure. No area has the ground-glass appearance.

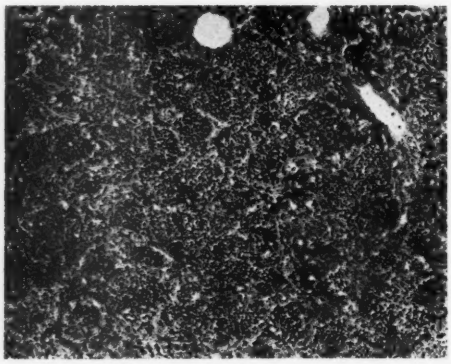

Fig. 10. Microscopic appearance of a pneumonic area of the specimen of Figure 9. The alveoli are filled with polymorphonuclear leukocytes, and three air-pockets are present. The neighboring regions, not shown in the illustration, present alveoli containing both clear fluid and air. No alveoli were collapsed (atelectatic).

types of x-ray films so obtained were studied and compared as to composition.

Ground-glass Shadow.—Many of the characteristics of the roentgen shadows of animal tissues which result from the presence of air within the tissues are generally well appreciated, although the physical explanation of these effects is not entirely understood. Thus, a pocket of air in the tissues appears as a "negative shadow," and diffuse infiltration with air causes the tissues to take on a general increase in radiolucence. These phenomena are commonly explained by reference to the great difference in atomic weight between the tissues and the air, and to the displacement of the tissues by air; but recent work (21) shows that the increase in radiolucence is greater by far than can be accounted for by these or other known physical principles. Whatever the explanation is, the phenomena are fundamental to pulmonary roentgenography and account for the exquisitely defined markings of the bronchial and vascular arborizations which appear in the shadows of normal lungs (Fig. 1-*B*), as well as for the clarity of delineation of foci of consolidation in otherwise air-filled lungs (Fig. 9). It is not generally appreciated, perhaps, that amounts of air in the tissues, so small as to be undetectable with other methods of gross examination and disclosed otherwise only by aid of the microscope, are plainly revealed with roentgenography. This point bears especially upon the present subject, as will appear later. Only when the tissues are entirely free from infiltration with air is their shadow homogeneous. The totally airless lung has the same uniformity of consistency of shadow (Fig. 1-*A*) as does the liver, spleen, kidney, or any other mass of solid soft tissue of a single composition. The density of the shadow, of course, depends upon the total thickness of the organ. Therefore, every thoracic roentgenogram contains examples of the appearances of the completely airless lung—the shadow of the subcutaneous tissue at the profiles of the chest, neck, and shoulders resembling that of the thin airless lung, and the shadow of the liver or heart being like that of the

Fig. 11. Lobar pneumonia (female, 29 years), 36 hours after the onset. The lower part of the right lung-field shows a fan-shaped shadow of streaks and mottlings, quite unlike ground-glass lung. The heart is slightly displaced toward the lesion and the right hemidiaphragm is elevated.

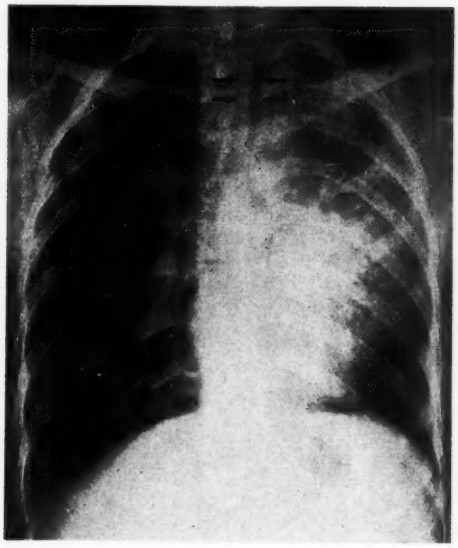

Fig. 12. "Fibroid" tuberculosis of the whole left lung and of part of the right upper lobe (male, 25 years) two years after the onset. The lesions are represented by discrete and confluent mottlings and streaks and there is no ground-glass sign. The heart and trachea are drawn toward the side with the larger lesion, and the hemidiaphragm on that side is slightly raised.

thick airless lung. The appearance is best described by likening the x-ray film in that region to a pane of glass with finely ground unpolished surfaces—whence the name, "ground-glass" shadow.

Our observations have shown that the shadow of an area of atelectasis—congential, obstructive, or compressive, in dog or in man—always exhibits the ground-glass roentgen shadow, provided: (1) that the dosage of x-rays is such as to obtain penetration of the tissues and demonstration of their radio-consistency (which is usually the case with the standard thoracic roentgenogram), and (2) that the shadow of the lesion is large enough to permit discernment of its consistency. On the other hand, many of the common consolidating lesions of the lung which are confused with atelectasis present a distinctly heterogeneous consistency of shadow because of residual air. Some lesions besides atelectasis present ground-glass shadows but these are usually distinguished readily from the presence of other signs. In short, the ground-glass sign enters into the diagnosis of pulmonary lesions to the extent that it indicates *complete* airlessness of the field ordinarily occupied by the lung or of such part of that field as is large enough for the composition of the roentgen shadow to be recognized.

Degree of Pulmonary Shrinkage.—Recent measurements by Wang and Van Allen (22) agree with the qualitative observations by many others, that a completely ateletatic division of the lung is very much smaller than normal, at either inspiration or expiration. Van Allen and Wu (23) measured the volumes of dogs' lung lobes which had been inoculated with pneumococci during life and been allowed to develop pneumonia. They found, pertinent to the present subject, that the volume was about normal at expiration and very frequently much

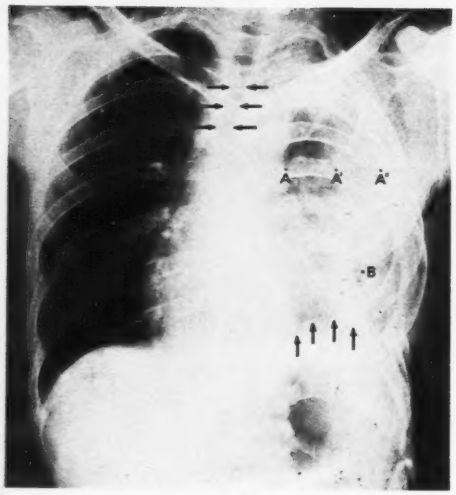

Fig. 13. Chronic empyema, with great thickening of the pleura and a very small cavity (male, 21 years), resulting from a gunshot three years before. It had been drained externally but failed to heal because of a retained foreign body. A solid body of thickened pleura (A'—A'') occupies the lateral half of the left lung-field and exhibits the ground-glass sign. The partially compressed, hypoventilated lung (A—A') lies in the medial half of the field, with a shadow that is less dense, mottled, and streaked. The cavity is at B. The spine is curved to the left, the intercostal spaces on that side are narrowed, and the hemidiaphragm is lifted, but the heart is pushed toward the other side.

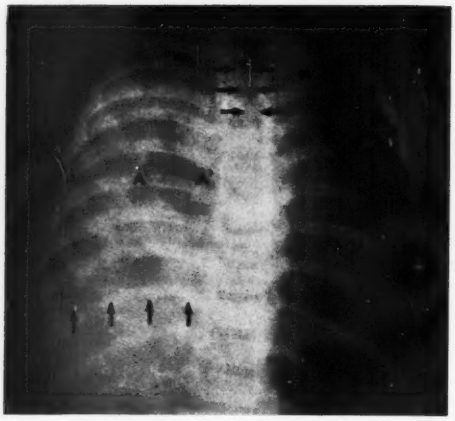

Fig. 14. Lobar pneumonia of the entire right lung complicated by acute empyema (female, 2 years), 14 days after the beginning of symptoms. The pus presents a ground-glass shadow in the lateral half of the right lung-field (A—A'), while the consolidated lung casts a mottled shadow in the medial half (A'—A''). The intercostal spaces on the right are narrowed, but the corresponding hemidiaphragm is very slightly depressed and the heart and trachea are pushed toward the other side.

smaller than normal at inspiration. The abnormality of volume at inspiration was most pronounced at the stages of the infection before development of consolidation and after complete resolution of the consolidation, and it was least pronounced during the height of consolidation. The shrinkage was not due to atelectasis, since none was present, but it was thought to be due to increased elastic tension of the parenchyma caused by the thickening of the alveolar septa that was present during all stages of this pulmonary inflammation. The increased tension brought about increased resistance to expansion of the inflamed part of the lung and this caused that part to be smaller than normal at inspiration. Later Wu (18) found these size relationships in man also, for thoracic roentgenograms showed an abnormally high position of the hemidiaphragm on the side of the lesion in the majority of the cases at inspiration but never at expiration.

It follows that a point of differentiation may be expected to appear in clinical roentgenography between atelectasis and pneumonia, if the diaphragm is examined at expiration as well as at inspiration; namely, in atelectasis elevation of the hemidiaphragm on the side of the lesion should occur at both phases of respiration, whereas in pneumonia it occurs, if at all, at inspiration only.

Clinical Results.—The application which we have found in the diagnosis of atelectasis for the ground-glass sign and for these factors of pulmonary shrinkage, taken together with the other diagnositic signs of atelectasis, is given in the following paragraphs. The diagnosis of the disease has become distinctly improved in accuracy during the two years during which these principles have been in use.

DIFFERENTIAL DIAGNOSIS

Massive Atelectasis.—The roentgen shadow of a massive area of atelectasis has

the consistency of ground-glass, unless shadows of irregular density are superimposed thereon. Accordingly, the sign is obtained in clinical roentgenograms only in the intercostal spaces and in areas in which the atelectasis involves the full thickness of the lung. The density is greater at the hilic region than at the periphery (Fig. 2), and in lungs containing more interstitial fluids than in those containing less (Figs. 3 and 4). Close scrutiny may be required to recognize the ground-glass quality in the denser shadows, but that quality in the lighter ones is very obvious. The borders of areas of ground-glass lung may be sharp, or they may be indistinct or totally lost because of fusion with neighboring shadows of similar consistency, principally the shadows of the heart and liver. The sign applies to all three types of atelectasis alike (Figs. 2, 4, and 8). It often represents the only diagnostic criterion of the disease, especially in compressive atelectasis and in symmetrically distributed, obstructive, or congenital atelectasis. In asymmetrically distributed, obstructive, or congenital atelectasis the ground-glass sign is accompanied by visceral dislocations of the kind peculiar to atelectasis, which were described in the introduction to this paper, and *the dislocations occur at both inspiration and expiration*. The shape of the shadow is characteristic when the lesion is due to obstruction of a single bronchus, for then the shadow fills the distribution of one bronchus, be it one whole lobe (Figs. 2 and 18) or a triangular segment of one lobe (Fig. 16); but oftentimes the shadow corresponds in shape to no units of pulmonary structure, as, for example, with multiple peripheral bronchiolar obstructions when the shadow occupies a zone along the profile of the lung (Fig. 15), and with pulmonary compression when the shadow conforms to the zone of the pressure upon the lung that happens to be in effect.

Focal Atelectasis.—The shadow of a part of the lungs which is involved with multiple focal atelectatic lesions presents scattered mottlings, cloudings, and streaks, which marks correspond to the positions of the individual foci of alveolar collapse. The ground-glass sign is absent. Focal atelectasis occurs in pure form most frequently in the compressive and congenital types of the disease. The compressive focal lesion is seen in lungs which are held partially collapsed for long periods, as frequently occurs in "mantle" pneumothorax, and the congenital focal lesion occurs very transiently in the process of expansion of the lungs of the new-born infant (Figs. 7 and 8). In both, the markings are usually "hard" and lie on a rather radiolucent background. Furthermore, in the congenital lesion, they tend to be arranged in lines radiating from the hilus. Focal atelectasis occurs very often in combination with various forms of pulmonary inflammation. Thus, the majority of cases of post-operative atelectasis are of the focal form; but here the entire involved region is usually fairly dark and

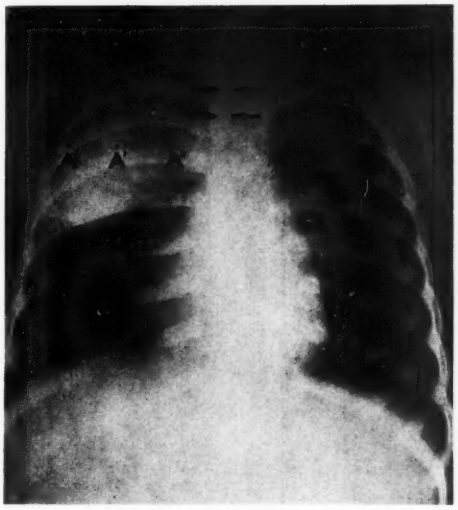

Fig. 15. Massive obstructive atelectasis, with cortical distribution accompanying lobar pneumonia of the right upper lobe (male, 3 years) four days after onset of illness. The lateral third of the right upper lobe (A—A') gives the ground-glass appearance of atelectasis, while the remainder of the lobe (A'—A'') shows the mottled shadow of pneumonia. The trachea and heart are displaced toward the lesion. Compare with Figure 16.

the mottlings, cloudings, or streaks in the lung-field are hazy and indistinctly separated from one another (Figs. 5 and 6).[3] As the disease progresses, the markings in a part or all of the area may become completely confluent and the ground-glass sign appears; but then, of course, the lesion is partly or wholly one of massive atelectasis. More concerning the composite lesions will be written below. Visceral displacements of the kind denoting reduction in the size of the lung occur with focal atelectasis under the same conditions as with massive atelectasis, *i.e.*, at *both inspiration and expiration* and when the lesions are obstructive or congenital and unilaterally predominant.

Pneumonia.—The roentgen shadow of a pneumonic area of lung, whatever the type or stage of the pneumonia, is practically always heterogeneous in composition because of the air that is scattered throughout the lesion.[4] The congestion and consolidation of early broncho- or lobar pneumonia are indicated roentgenographically by hazy streaks or mottlings in the lung-field (Figs. 9 and 11), which are sometimes very similar to the markings in focal atelectasis. As the consolidation spreads, these opacities increase in number, size, and density and become more and more confluent; but, even at the height of the disease, careful scrutiny discloses faint cloudings or mottlings rather than a completely uniform and ground-glass shadow. The ground-glass appearance occurs rarely, and only in markedly chronic pneumonias. Visceral displacements in pneumonia indicating reduction in the size of the lung are either entirely lacking or are *confined to inspiration.* The diaphragm is usually the only structure dislocated. The differentiation between pneumonia and atelectasis, when each is in pure form, is thus quite easy: Pneumonia is distinguished from massive atelectasis by the lack of the ground-glass sign, and from focal atelectasis by the lack at expiration of such visceral displacements as are caused by reduction in pulmonary size.

Tuberculosis.—It is as true of tuberculosis as of pneumonia, that the affected portion of the lung contains some, though a reduced amount, of air and casts a heterogeneous roentgen shadow (Figs. 12 and 18). To be sure, uniformly caseous areas are totally airless, but these are rarely large enough to give the ground-glass shadow. The denser lesions may show no other irregularity of composition than faint clouds, but, even so, their shadows are clearly not of ground-glass quality. Small scattered tuberculous lesions often show markings that are readily mistakable for those of focal atelectasis. In cases in which visceral displacements are lacking, obstructive focal atelectasis is ruled out; but where such displacements occur, at both inspiration and expiration, as they often do from the contraction of fibrous tissue in the lung, it may be difficult or impossible to distinguish tuberculosis from focal atelectasis by means of roentgenography alone. Under these circumstances, of course, obstructive focal atelectasis (that is, in its pure form) can be ruled out usually from the fact that it seldom, if ever, occurs so chronically as does tuberculosis. Conversely, when the lung is partially compressed, as with mantle pneumothorax, and compressive focal atelectasis develops therein, it may be impossible to distinguish the condition from tuberculosis. This much may be said rather categorically of the differentiation of these two diseases: The lack of the ground-glass sign rules out massive atelectasis, and the lack of visceral displacements eliminates obstructive focal atelectasis.

Hemorrhagic Infarction.—The roentgen-shadow of an infarct is almost always heterogeneous in consistency owing to the presence of smaller or larger amounts of

[3] The general density and haziness are due to the acute inflammation that nearly always accompanies the lesion in these patients, in the form of edema, bronchopneumonia, or both. The special rôle of this inflammation in the pathogenesis of postoperative atelectasis is explained in another publication (24).

[4] Histologic examination of the consolidated tissues in pneumonia, even at the height of the lobar disease, usually reveals scattered bubbles of air. These may be small and sparse, but *in toto* they disturb very distinctly the uniformity of composition of the roentgen shadow. The air remains throughout the course of acute pneumonia, probably because the blood supply, upon which its absorption depends, is very poor.

air in the tissues.[5] The shadow is mottled or streaked, and the amount and degree of such opacity are determined not only by the quantity of blood and other fluids extravasated in the lung, but also by the presence and amount of atelectasis and fibrosis.[6] The latter lesions sometimes produce sufficient pulmonary shrinkage to cause environmental displacements at both inspiration and expiration. This is more frequent in infarcts of several months' duration. When fibrosis and atelectasis are lacking, the displacements are also lacking and the lesion is thereby distinguished from atelectasis. Otherwise, hemorrhagic infarcts are known from massive atelectasis by the absence of the ground-glass sign, and from pure obstructive focal atelectasis by the great rarity of chronic lesions of the latter type.

Neoplasm.—When the air is displaced totally from a portion of the lung by infiltration with tumor cells, the roentgen shadow of the region presents the ground-glass sign—that is, if the area is large enough and if air-containing parenchyma is not superimposed thereon. These two conditions are not often present, but even when they are, neoplasm in pure form is readily distinguished from massive atelectasis by the absence of the environmental displacements characterizing the latter disease. (See below for neoplasm associated with atelectasis.)

Pulmonary Hypoventilation.—Owing to the partially collapsed state of the parenchyma in pulmonary hypoventilation, the normal markings of the lung are brought closely together and present a mottled appearance that is often just like that of pure focal atelectasis (Fig. 4). Indeed, when the lung has been partially collapsed for days or weeks, both pulmonary hypoventilation and compressive focal atelectasis are often present and the differentiation is impossible. Of course, visceral displacements are of no assistance. However, pulmonary hypoventilation always can be told from massive atelectasis from the lack of the ground-glass shadow.

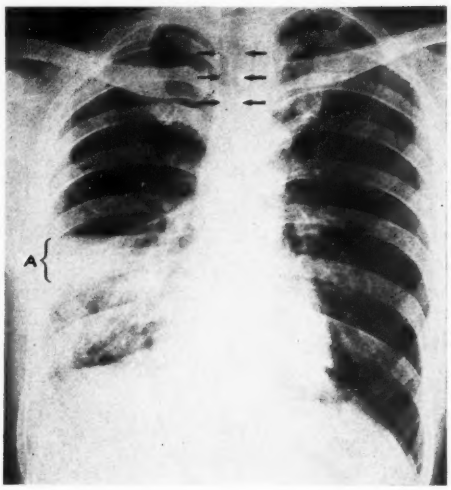

Fig. 16. Massive obstructive atelectasis associated with unresolved pneumonia of the right lower and middle lobes (male, 40 years) six weeks after onset of symptoms. The upper outer quadrant (*A*) of the affected field gives the ground-glass shadow of atelectasis, while the remainder gives the mottled and streaked shadow of pneumonia. The mediastinal structures are shifted to the side of the lesion.

Extra-pulmonary Lesions.—Any extra-pulmonary mass that encroaches upon the lung-field and is uniformly and moderately radiopaque, like a collection of intrapleural fluid or thickened pleura, gives a ground-glass shadow, provided, of course, that it is thick enough and does not lie over air-containing lung. Because of the last requirement, these masses present the sign only when they occupy the full depth of the pulmonary space and this occurs most often at the profiles of the lung-field (Figs. 13 and 14). They are readily distinguished by the x-ray from massive atelectasis when, as is usual, they lack environmental displacements of the type and extent characteristic of atelectasis; but when such displacements do occur, as in chronic pleurisy with extensive fibrosis, from the contraction of the fi-

[5] Bubbles of air are captured in the alveoli at the occurrence of infarction by the influx of red cells and serum. They tend to remain there for very long periods, probably because the blood supply is extremely poor (25).

[6] In many hemorrhagic infarcts, foci of atelectasis develop first from blockage of the air passages with blood cells and desquamated epithelium and later from fibrosis (25).

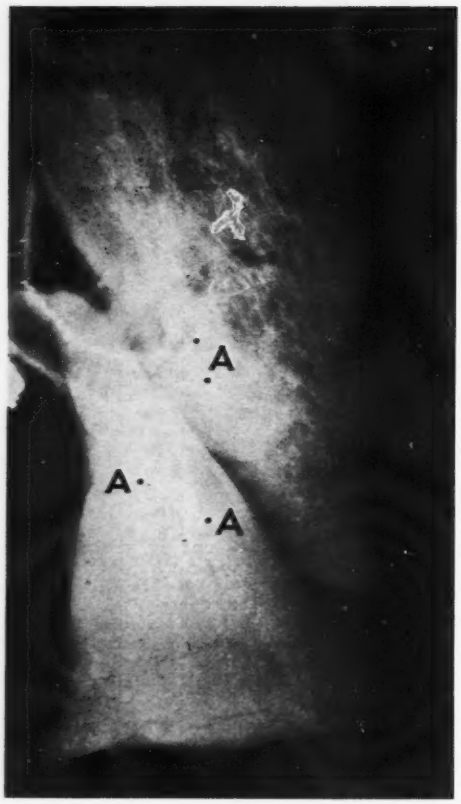

Fig. 17. Massive obstructive atelectasis and pneumonia in the left lung taken from a man (45 years) who died one week after gastro-enterostomy and five days after onset of acute respiratory symptoms. The lower lobe is shrunken and presents the ground-glass sign of atelectasis, except at points where calcareous bronchial plaques cast dense shadows (*A*). The lower fourth of the upper lobe is also atelectatic and has the same appearance, but the remainder of that lobe is pneumonic and mottled. (Reproduced by permission of Dr. Edward D. Churchill.)

brous tissue, the roentgenographic appearances may be quite like those of massive obstructive atelectasis of cortical distribution.[7] However, in the great majority of these extra-pleural masses, the viscera in the neighborhood of the lungs are either not displaced at all or are dislocated in a different direction than in atelectasis.

Composite Lesions.—When massive atelectasis and another consolidative disease occupy the same portion of the lung—that is, when they are superimposed upon each other—the ground-glass shadow of atelectasis appears over the whole area and obliterates all marks of the other lesion (Figs. 3, 4, 15, and 16); unless masses such as calcific deposits (Fig. 17) or air-filled cavities (Fig. 18), which are of distinctly different density from the airless pulmonary tissues, are present to indicate the existence of the second lesion. The markings of pneumonia and of tuberculosis are effaced most often by the superimposition of massive atelectasis. Of course, when any part of the inflammatory field is left without atelectasis, the lung markings characteristic of the inflammation appear in that region side by side with the ground-glass shadow of the atelectasis (Figs. 15 and 16).

When lesions of focal atelectasis form in a field containing small bronchopneumonic foci, the composition of the shadow does not indicate the fact, but the presence of environmental displacements of the type and extent characteristic of atelectasis does so. Focal atelectasis in a field occupied by tuberculosis[8] is well-nigh un-

[7] We know of several cases of pneumonia in children in which the differentiation between a local collection of pleural fluid and cortical atelectasis was possible only by thoracentesis. In one case reported to us, cortical atelectasis was mistaken for empyema and thoractomy by rib-resection was actually done; but there the mistake could have been prevented by noting and correctly interpreting the presence of the visceral shift typical of atelectasis.

[8] Compressive and obstructive atelectasis, of both focal and massive forms, develops very often in association with pulmonary tuberculosis. The compressive type is practically always secondary to pneumothorax or other cause of local pulmonary compression. Bronchial obstruction is common in tuberculosis, for the infection often begins by involving the lymphoid patches in, or close beside, the tertiary bronchi (26) and produces swelling, caseation, ulceration, and cicatrization (with healing) of the bronchial wall. Van Allen and Ch'in (27), by examining a few lungs of man at autopsy, have been able to find several examples of peripheral bronchi abruptly obliterated at points at which they passed through small healed tuberculous lesions. In these cases, as probably also in the great majority of all instances of obstruction in tuberculosis, the lobule of the obliterated bronchus was not atelectatic but fully air-containing owing to collateral respiration (28, 29). But where inflammatory swelling (here tuberculous) of the parenchyma interferes with collateral respiration (24), atelectasis must develop, being focal in form where small bronchi are blocked and massive where large bronchi are blocked.

We believe that many of the tuberculous lesions that are diagnosed as fibroid because of pronounced pulmonary shrinkage present that quality because of the presence in the lesions of many small foci of atelectasis, rather than because of the contraction of fibrous tissue, as is commonly thought. This belief is entertained because in many cases the lung returns to normal size coincidently with healing. The return to normal size is readily explainable by reinflation of the atelectatic foci by collateral respiration (30), whereas scar tissue would cause permanent or, at least, long enduring pulmonary shrinkage.

recognizable roentgenographically, since the composition of the shadow is not appreciably different and since the environmental dislocation produced by the atelectasis does not help, appearing as it does also in tuberculosis without atelectasis.[9]

When neoplasms of the lung are associated with atelectasis, from obstruction of bronchi or from compression of the parenchyma by the tumor, or from both causes, the shadows of the two lesions are fused and indistinguishable. The tumor may then be unrecognizable as such, or, if detected, it may appear much larger than it really is. At least the presence of the obstructive atelectasis is indicated by the occurrence of environmental displacements of the atelectatic type (Fig. 2), but even the presence of compressive atelectasis is frequently undetectable roentgenographically. We know of no way to overcome these difficulties.

Intrapleural accumulations of fluid or masses of thickened pleura lying at the profiles of the lung-field often seem thicker than they actually are, because they compress the cortex of the lung and produce a layer of massive atelectasis that adds to the width of the ground-glass roentgen shadow. Displacement of environmental viscera does not enter to assist the diagnosis. This source of error seems to have no remedy.

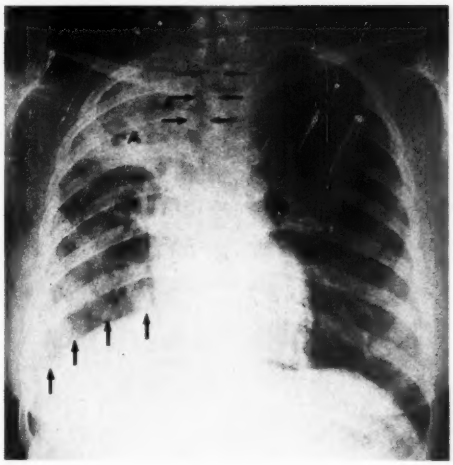

Fig. 18. Massive obstructive atelectasis of the right upper lobe superimposed upon chronic fibroid tuberculosis (female, 20 years) two years after onset. The upper lobe presents the ground-glass appearance of atelectasis except where "negative shadows" mark the positions of cavities (*A*), while the field below shows the heterogeneous shadow of tuberculosis. The mediastinal structures are drawn toward the right and the corresponding hemidiaphragm is lifted.

SUMMARY

The difficulties and fallacies in the roentgen diagnosis of atelectasis are recounted and shown to be due largely to two causes: Lack of agreement in the definition of atelectasis and lack of pathognomonic signs. The preference of the authors as to terms is stated, and a new sign, "ground-glass" lung, which was discovered as a result of a special investigation, is described and explained. Also, some recently acquired facts as to the degree of shrinkage of the diseased section of the lungs in pneumonia as compared to that in atelectasis are introduced. The differential diagnosis of atelectasis is then outlined, with special reference to the manner of use of the ground-glass lung and of the degree of pulmonary shrinkage.

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CHANGES IN ELECTRIC POTENTIALS AND RATES OF OXIDATION OF THE SKIN SUBSEQUENT TO ROENTGEN IRRADIATION[1]

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IN most of the experimental work which has been done on the effects of irradiation with roentgen rays on biologic materials, an end-effect only, or the effect at one definitely specified time after the irradiation, has been investigated. The purpose of the investigations now being reported was to determine the variations in the physiologic quantities of frog's skin, namely, the electric potential difference across the skin and the rate of consumption of oxygen of the skin as dependent on the time after irradiation. Other investigations have shown that there is some relation between the electric potentials and the rate of consumption of oxygen and that the magnitude of the potential difference may be taken as a "measure of life" or of the vitality of the skin. The literature regarding the correlation in living organisms between metabolic and electric gradients has been reviewed and additional evidence brought forth in papers by Child (3), Child and Hyman (4), and Hyman and Bellamy (8). The results of the more recent published researches will be given in résumé in a subsequent part of this paper.

EXPERIMENTAL PROCEDURE

In one of our series of experiments, measurements were made on the electric potential difference across sections of skin from both the dorsal and ventral surfaces of 125 non-irradiated, or control, frogs and 611 irradiated frogs, and on the rate of consumption of oxygen by sections of skin from the dorsal surface of 75 control and 185 irradiated frogs. The irradiated frogs received a dose of 9,000 roentgens of unfiltered roentgen rays. The effective wave length (Duane, 6), as measured by the absorption in 0.1 millimeter of aluminum, was 0.64 Ångstrom and the half value layer of aluminum was 0.67 millimeter. The intensity of the radiation, when the chamber was placed underneath the frogs, was 42.5 per cent as great as with the chamber on the surface.

In the second series of experiments, measurements were made on the potential differences across sections of skin from the dorsal and ventral surfaces of 22 control frogs and 45 frogs which had received a dose of 160,000 roentgens of unfiltered roentgen rays. Following irradiation the frogs were kept alive until the time at which it was desired to make the measurements. The irradiated frogs in the first series were divided into 21 groups, each group being used in these experiments at a different time, varying from three and a half hours to thirty days after irradiation. The irradiated frogs of the second series were divided into five groups which were used on different days from the first to the eleventh day after irradiation. A dose of 9,000 roentgens had no visible effect on the frogs. Doses of roentgen rays of 160,000 roentgens were fatal in from eleven to fourteen days.

Sections of skin from three to six frogs were used in a single experiment, one of the frogs generally being non-irradiated and serving as a control. After pithing, the skin was removed, washed in Ringer's solution, and sections of the dorsal and ventral skins put in the cells for the measurement of potential difference. The method of measuring the electric differences of potential was the same as reported previously by Williams (25) except that salt bridges and calomel half-cells were used

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instead of electrodes of zinc-zinc sulphate for the connections between the cells and the potentiometric system. The water bath was kept at a constant temperature of 35° C., instead of 25° C. as in the previous investigation.

Adjacent sections of skin were put in the modified Krogh manometers (Krogh, 11, and Bodine and Orr, 2) for measuring the rate of consumption of oxygen. The stopcocks on the manometers were closed and the first readings of the potential differences were made forty-five minutes after the frogs were pithed. Readings were taken on both the potential differences and on the manometers every fifteen minutes until the end of the third hour after pithing, every half-hour for the next hour, and every hour until the end of the tenth hour. At the conclusion of each series of readings the sections of skin in the manometers were weighed and the rate of consumption of oxygen was calculated in cubic millimeters per minute for each milligram of weight of skin.

The average value of the potential difference for the first ten hours after pithing and the average rate of consumption of oxygen for the first three hours were used as the basis for the making of all comparisons. Due to seasonal variations which were found to arise experimentally in the values of both the potential differences and rates of consumption of oxygen, we compared the data obtained from any specified irradiated group with the data obtained from controls at about the same time.

EXPERIMENTAL RESULTS

At the end of three and a half hours after irradiation with 9,000 roentgens the value of the potential difference across the surfaces of both the dorsal and ventral skins had increased to a value greater than that of the controls. Curves 1 and 2, Fig. 1, and Table I show that the values of the potential difference continued to increase and became maximal on the second day for the dorsal skin and on the third day for the ventral skin. Following this initial period of increase, the values for the potential differences decreased rather suddenly on the day following the maximal value and from then on more slowly until the ninth or tenth day. On the tenth day the value for the ventral skin increased to a maximum during the second period of increase of values of the potential difference and remained high for three days, dropping on the thirteenth day to a value about the same as that of the controls. The second period of increase of potential difference for the dorsal skin occurred about a day later than for the ventral skin: on the fourteenth day the value dropped below that of the controls. The value of the potential difference for both surfaces reached a maximum for the third period of increase on the sixteenth day. The values for both ventral and dorsal skins fell below those of the controls on the eighteenth day: the value for the ventral skin continued to decrease until the twenty-second day and the value for the dorsal skin until the twenty-fifth day. After reaching these minimal values on the twenty-second and twenty-fifth days, both values gradually increased but were still below the values of the controls on the thirtieth day. The changes in the dorsal skin were relatively much greater and more sudden than those in the ventral skin. A difference in the effects on the two surfaces (ventral and dorsal) would be expected, since the dorsal skin is thicker and contains more glands and pigment than the ventral skin and the ventral skin received less than half the dose of roentgen rays received by the dorsal surface on account of the absorption of radiation by the bodies of the frogs.

The course of the changes in the rates of consumption of oxygen (Curve 3, Fig. 1 and Table I) of the dorsal skin was, in general, the same as occurred in the measurements on the potential differences across the sections of skin. These changes, however, preceded the changes in potential difference and were relatively smaller in general. The third period of increase of

consumption of oxygen lasted two days longer than the third period of increase of potential, reached a minimal value on the twenty-second day, and then increased quite slowly to the thirtieth day.

injury. The curves showing potential differences and rates of consumption of oxygen indicate that the skin of frogs, following an irradiation with a dose of 9,000 roentgens, passes through three

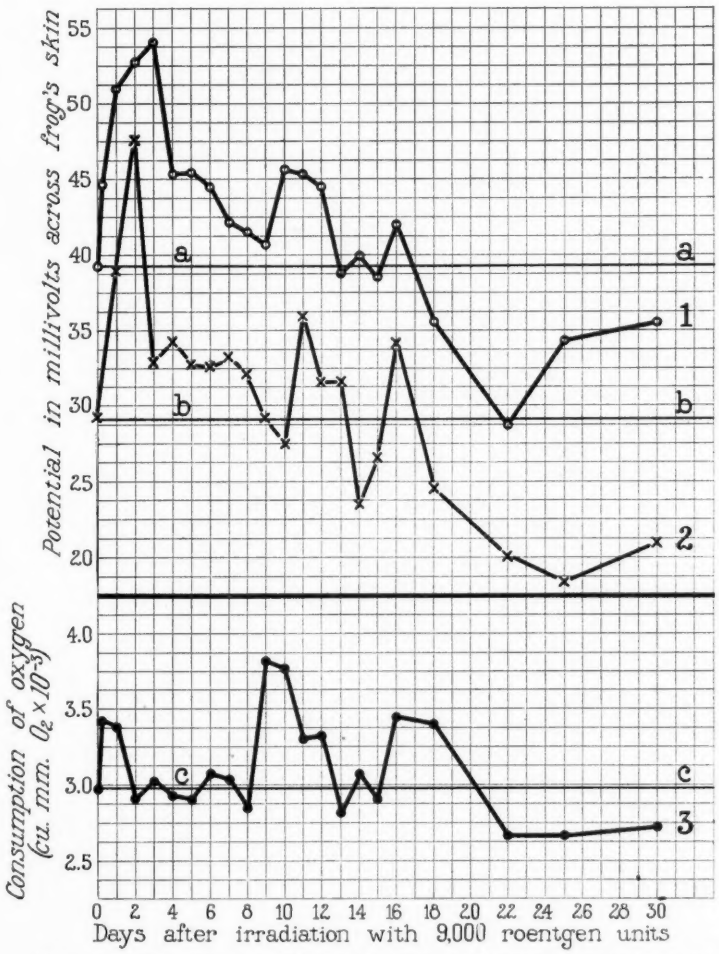

Fig. 1. Curve 1 shows the values of the potential differences across the ventral skin; Curve 2, across the dorsal skin, and Curve 3 the rate of consumption of oxygen for the dorsal skin on days subsequent to the irradiation of frogs with 9,000 roentgens of x-rays. The straight lines *a*, *b*, and *c* represent the corresponding average values for frogs used as controls.

The periods of increased potential and consumption of oxygen may be considered as periods of increased activity or vitality and the periods of decreased potential and consumption of oxygen may be regarded as periods of lowered vitality or of periods or cycles of increased activity. The ultimate effect, however, is that of injury; this becomes evident on about the eighteenth day. Recovery is still far from complete on the thirtieth day. The curves (Fig. 1) showing the relationship between

the time subsequent to irradiation and the values of the potential differences and rates of consumption of oxygen are quite similar to the curves showing the development of erythema in the human skin following roentgen irradiation (Miescher, 14, Harris, Leddy, and Sheard 7, Pohle 17, and others).

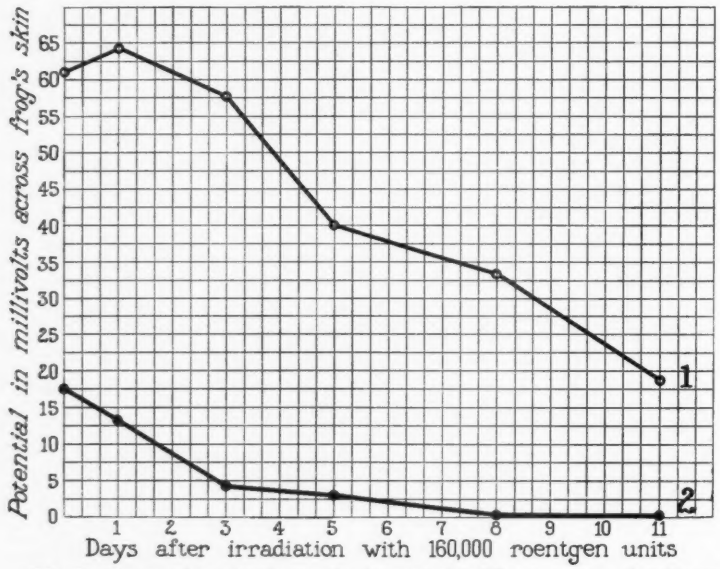

Fig. 2. Curves show the changes in the potential difference across the skin on days subsequent to irradiation with 160,000 roentgens of x-rays. Curve 1 is for the ventral skin and Curve 2 for the dorsal skin.

Figure 2 and Table II show that the potential difference across the dorsal skin is much lower in value on the first day subsequent to irradiation with 160,000 roentgens than the potential difference of the dorsal skin of the non-irradiated, or control, frogs and that it decreases rapidly until the eighth day. At the eighth day the potential difference across sections of the dorsal skin is practically zero, indicating that the skin is dead. The potential difference of the ventral skin is higher than the value of the controls on the first day, but falls below that of the controls by the third day and continues to decrease until death occurs on the eleventh to the fourteenth day. The period of increased vitality is less than three days for the ventral skin and less than one day (if not absent entirely) for the dorsal skin. Evidently the effect of a dose of 160,000 roentgens is definitely injurious to the skin. The cyclic type of reaction is not as evident after a dose of 160,000 roentgens as after a dose of 9,000, but there is some indication of its presence.

COMMENT

The conclusion may be drawn from various published researches that electric potential differences are associated quite definitely with metabolic gradients. Lund and Kenyon (13) found that, in the tips of roots, the region of active division of cells was electropositive to the more basal regions and that the region evidencing activity of cellular division also had the highest respiratory rate. In other papers, Lund (12) considered the subject of potential differences, such as arise across the surfaces of frog's skin, and concluded that there was a definite relationship between the potential difference and the

TABLE I

Average values for the potential differences across the ventral and dorsal skins from frogs and the average values of the rates of consumption of oxygen for the dorsal skin on days subsequent to irradiation with 9,000 roentgens

Time after Irradiation	Frogs in Group	Potential Difference (in Millivolts)		Rate of Consumption of Oxygen	
		Ventral Skin	Dorsal Skin	Frogs in Group	Value in Cubic Millimeters Each Minute, for Each Milligram Weight, $\times 10^{-3}$
Controls	125	39.0	28.5	75	2.97
3.5 hours	35	44.9	28.8	4	3.39
1 day	34	51.1	39.0	5	3.72
2 days	32	52.7	47.6	6	2.82
3 days	33	53.9	32.8	4	3.03
4 days	33	45.3	34.2	5	2.88
5 days	34	45.6	32.8	5	2.85
6 days	32	44.5	32.5	3	3.06
7 days	30	42.1	33.1	5	3.03
8 days	32	41.4	32.2	3	2.70
9 days	32	40.6	28.5	5	3.83
10 days	28	45.6	27.4	12	3.77
11 days	27	45.3	35.9	13	3.30
12 days	28	44.5	31.4	8	3.33
13 days	27	38.6	31.4	10	2.64
14 days	27	39.9	23.4	14	3.06
15 days	28	38.6	26.5	14	2.88
16 days	30	42.1	35.4	17	3.44
18 days	28	35.5	24.8	17	3.39
22 days	27	28.9	20.0	17	2.64
25 days	25	34.3	18.5	14	2.64
30 days	9	35.5	21.1	4	2.68

rate of oxygen consumption. Sheard and Johnson (22) showed that, in response to various qualities and quantities of radiant energy, there is a correlation between the electric potential differences developed across areas situated near the base and tip ends, respectively, of leaves intact with plants and the metabolic activities of such leaves. In 1931 Purdy, Johnson, and Sheard (18) reported that, in normal, healthy persons with normal circulation of the blood and normal physiologic functioning of the skin, there is a definite correlation between basal metabolism and cutaneous differences of electric potential. There is little doubt but that metabolic activity and potential differences are correlated and, therefore, that the electric potentials are dependent to a considerable extent on the rates of consumption of oxygen.

The correlation between the values of the potential differences and consumption of oxygen was not definite in the case of the samples of skins from frogs within a single group. There was a wide variation in potential differences, whereas the value of the rate of consumption of oxygen remained nearly constant. In general, however, a skin showing a high potential difference also evidenced a higher rate of consumption of oxygen. This finding would indicate that there are factors which may influence one of these quantities more than they do the other. A thicker skin, according to the theories of Lund, would have a greater potential difference than a thinner skin, and yet the rates of consumption of oxygen for each unit of weight of skin might be the same.

In portions of our experimental work there was evidence that there is a correlation between the potential differences and the consumption of oxygen. In eleven instances determinations were made of the consumption of oxygen by both the dorsal and ventral sections of skin. The ratio of the average values of the potential differences of the two surfaces was 1.48, in these eleven instances, and 1.36 for the ratio of consumptions of oxygen. This indicates that, for sections from the same frog but from different parts of the body, there is a correlation between the potentials and the

TABLE II

Average values of the potential differences across the ventral and dorsal skins from frogs on days subsequent to irradiation with 160,000 roentgens

Time after Irradiation	Frogs in Group	Potential Difference in Millivolts	
		Ventral Skin	Dorsal Skin
Controls	22	60.5	17.6
1 day	10	64.0	13.5
3 days	11	57.7	4.0
5 days	10	39.9	2.8
8 days	8	33.4	0.14
11 days	6	18.7	0.09

consumption of oxygen. Furthermore, the course of the seasonal changes in electric potentials across sections of the skin is paralleled quite closely by the course of the consumption of oxygen, again indicating a correlation between potential differences and consumption of oxygen.

The effects of irradiation on metabolism and the rate of consumption of oxygen have been investigated by several. Redfield and Bright (19) found that irradiation of radish seeds caused an increase in the rate of production of carbon dioxide. Jugenburg (9) found that irradiation caused either an increase or decrease in the basic metabolic rates of guinea pigs, depending on the portion of the body irradiated. Wehmer (24) found that irradiation caused an increase in the rate of consumption of oxygen of frog's muscle. Although his data are not very complete, there is some indication that the course of consumption of oxygen followed a cyclic type of curve similar to the one presented in this article.

The changes in consumption of oxygen and the electric potential difference are due probably to the effects of irradiation on more than one property of the cell. Richards and Woodward (21) and Packard (15) have shown that irradiation may cause either a precipitation of or a breaking up into smaller particles of the colloids of protoplasm, and that it may activate or destroy some of the enzymes present. Dessauer (5) reported the denaturization of pseudoglobin by irradiation, causing particles to become visible in Brownian movement. The reaction was not constant, but appeared and disappeared and evidenced a cyclic type of effect.

One of the chief effects of irradiation must be concerned with some controlling mechanism. This type of effect, while it might activate initially processes which would cause a temporary increase in function, would be primarily or eventually injurious to the cells. An effect on some controlling mechanism, and one which is primarily injurious to the cells, might explain the type of results we have obtained with large doses of roentgen rays. On this assumption, a decrease or absence of a period of increased activity caused by larger doses of radiation, as portrayed in Figure 2, would be due to an initial injury of so great a magnitude that the injurious effects would become evident shortly after irradiation. It would appear that ultimately roentgen irradiation must be injurious to the cells, although initially, under certain conditions of dosage, such irradiation might instigate changes of a chemical and physical character (such as changes in permeability of cells, charges on the surfaces, and increased ionization) which would indicate a temporary state of increased activity.

The cyclic type of reaction following irradiation may be due in part to cellular processes which counteract or repair the injurious effects which have been produced by irradiation. Oxidative processes which are proceeding at an abnormal rate may bring into play other reactions which tend to inhibit the rate of oxidation. After this has occurred, the inhibitory agent may cease to exert its influence and

the tendency toward an abnormal rate again may become evident. It is also possible that all of the periods of increased activity may not be produced by the same underlying cause.

Kingery (10), Pfahler (16), and Stenstrom and Mattick (23), who investigated the effects of irradiation on the human skin, suggest that the effect is at its maximal value at the end of the period of irradiation and that, from the time of irradiation, the effect in the skin decreases according to the logarithmic law. As to just what constitutes the primary effect of irradiation in the skin is not known definitely. However, it is probable that this primary effect, whatever it may be, would be at its maximum at the end of the period of irradiation and, therefore, it is a reasonable assumption that the primary effect would decrease with time following irradiation.

While it is a logical assumption to postulate that the primary effect of irradiation decreases logarithmically following irradiation, there is little if any experimental evidence to show that it does so. On the other hand, if the physiologic effects *in toto*, or as measured by certain processes which are taking place within the cells, are considered, there is direct experimental evidence that the effects of irradiation appear in cycles and that the maximal value may occur long after irradiation. Miescher (14), Bachem (1), Reisner and Neeff (20), and Harris, Leddy, and Sheard (7) have investigated the cyclic appearance of the erythema and the course of the pigmentation of the skin following irradiation. Pohle (17) obtained the same type of curves for the changes in color and from a study of the capillaries showed that there is a correlation between the changes in color of the skin and the number and sizes of the capillaries visible under the microscope. These and similar results indicate quite definitely that the physiologic effects of irradiation occur in cycles or rhythmically, at least for a considerable period after irradiation and prior to the time at which injurious effects are evident.

SUMMARY

Measurements were made on the potential differences across sections of frog's skin and on the rates of oxygen consumption of skin prior to and after irradiation with roentgen radiation.

There was a seasonal variation in both the potential differences and the rates of consumption of oxygen which paralleled the degree of metabolic activity.

After irradiation with a dose of 9,000 roentgens, both the consumption of oxygen and the potential differences were increased, in general, for from sixteen to eighteen days. The increase was not constant but followed a cyclic type of reaction somewhat similar to the curves of erythema produced in human skin by roentgen irradiation.

Following this period of general increase, the values for both the potential differences and the consumption of oxygen decreased to values below those exhibited normally and remained below normal on the thirtieth day subsequent to irradiation.

In general, the courses of the curves showing the values of the potential differences and the consumption of oxygen were similar, but the changes in rates of consumption of oxygen generally preceded the changes in the potential differences.

The changes in both potentials and consumption of oxygen were more rapid and of greater magnitude in the dorsal skin than similar changes in the ventral skin.

Employing a lethal dose of 160,000 roentgens, the period of increased activity was abbreviated, being less than three days for the ventral skin and less than one day (if not entirely absent) for the dorsal skin. The cyclic type of effect was not pronounced. The injurious effect on the dorsal skin was of much greater magnitude than in the case of the ventral skin.

In general, these investigations indicate that the effects produced by irradiation with roentgen rays on the differences of electric potentials and rates of consumption of oxygen of the skin are portrayed chronologically, subsequent to irradiation, as cyclic types of reaction.

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CORRELATING ANATOMY AND ROENTGENOLOGY[1]

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THE student of medicine, whether undergraduate or practising physician, although he may have no interest in clinical roentgenology, is vitally concerned with the living body; and, therefore, dependent upon the technics of roentgenology which teach us so much about the living. In human anatomy we desire to know the living structure and the gross function of the body, and anatomy has been pursued in the classical way to gain this knowledge. This desire agrees with the best anatomical tradition, beginning with Vesalius, yet in most medical schools, no matter what the pronouncements about inadequacies of dead anatomy, the terms "anatomy" and "dissecting" are still synonymous. Obviously, fabrics of the body may be learned in the dissecting room but the topographic anatomy of the living must be learned from the living. That part of physiology which the physiologists do not claim and which has, therefore, remained with anatomy—the function of muscle groups, the action of joints, the mechanics of the chest—is likewise not a cadaver study. Anatomy to medical students and to physicians should mean a study of the living body by any means. Naturally dissection has played a significant rôle in this study and must continue to do so, but it should not be emphasized at the expense of exclusion of other methods. I explain to my students that in anatomy we study the body by any technic which yields knowledge. Certain facts may be obtained only by dissection but many of these facts are useless unless vitalized. In the vitalization, the radiologic laboratory helps us most.

I have taught first-year medical students and first-year dental students and I am now teaching graduate doctors, preparing for special fields of practice. I have excellent opportunity to obtain a bird's-eye view of the results of medical school teaching in anatomy and I am more convinced than ever that the teaching of anatomy must be in fact the teaching of the anatomy of the living. In the following remarks, I shall draw on my experiences, especially those obtained in the Department of Anatomy in the University of Cincinnati, where, by trial and error, I developed certain teaching methods which enabled me, even in the crowded medical curriculum, to present the anatomy of the living. This technic, as it concerns the use of the radiologic laboratory, will be described in some detail, because I find that the teaching value of the fluoroscopic screen and the roentgen film varies with the aptness of the presentation.

My ideas about the use of roentgenologic facilities in anatomy were gradually shaped during five years of experimentation with the x-ray as a teaching aid. In this trial period, I found that it was not profitable to put view boxes into the corridors or into the dissecting rooms, with films changing from week to week. As long as the instructor looked at the films, the student looked. I think that the reason for this is obvious: the student did not understand how to see. Similarly, when the students went to a hospital fluoroscopic laboratory, because the roentgenologist did not know each student's background and because he was not an integral and constant part of the teaching program, the demonstrations were not properly correlated.

In introducing the students to the study of anatomy, a brief survey of the skeleton helps in acquiring terminology. This pe-

[1] Read before the Radiological Society of North America, at the Seventeenth Annual Meeting, at St. Louis, Nov. 30–Dec. 4, 1931.

riod is short, because the skeleton should not be studied as dissociated from the other parts of the body.

During the first week, the students also study the first film, a roentgenogram of a single cervical vertebra. In small groups of four or five, they are shown how, point for point, the dry vertebra from which the roentgenogram was made can be identified on the film. This is repeated a sufficient number of times so that it is possible for every one in the group to trace the outline on the film. Next, a series of cervical vertebræ is examined with its roentgenogram. When the students become familiar with the problem of over-lapping and are able to pick out the outlines of any one vertebra, they are then shown the films of the living neck and are asked to identify the parts of the vertebra. Sometimes this consideration of the roentgen anatomy is preceded by a general discussion of the production of x-ray shadows. It is probably more effective, however, to present these problems as they come up in the actual use of the films, giving only the bare preliminary information that the x-radiation is stopped by certain tissues and that the x-radiation influences photographic films and certain fluorescent materials.

It will be readily appreciated that, with a class of from seventy to a hundred students, demonstrations to groups of four or five mean a tremendous amount of personal teaching. I believe that this must be done, however, for it enables the teacher or his assistant to clear up questions that arise. In the very first week, then, of the medical course, my students had seen and had identified the parts of the vertebral column of a roentgenogram taken of the living.

It is not the purpose of the anatomic laboratory to teach the practice of roentgenology. The Department of Anatomy undertakes to give the students just so much of the technic of roentgenology as will enable them to see the structures accurately. In other words, they are being instructed in a new method of seeing. They must learn to distinguish three dimensions from two. Students are helped to pick out the outlines of those normal structures with which they are familiar. No effort is made to interpret disease processes unless they obtrude.

The second demonstration to the students is based upon the thorax, using the dry mounted skeleton, flat films of the chest, and stereoscopic films in a duplex stereoscope. With this material, two students with an instructor study the films until the latter is sure that each student has seen the chest in the round and is able to pick out the ribs anteriorly and posteriorly in the thoracic cage. This demonstration is more time-consuming than the first one, because the groups are smaller and there always are two or three in any class who have difficulty with stereoscopic vision.

The students by this time have had sufficient experience profitably to spend time looking at films. To supply this urge and to check up deficiencies, an old teaching trick is used: homework is required. A series of reduced films with an 8×10-inch view box is loaned to each two students. Definite tracings are asked for, such as the outline of the skeleton as seen on the film in one, on a second a tracing of the outline of the soft parts, such as the heart and diaphragm. In the laboratory, view boxes of chest films are on display and the instructors go over the outlines of the heart borders on the dissected specimen to show the anatomic basis of the heart roentgen silhouette. After this has been done, the first fluoroscopic demonstration is held.

For this, groups of seven are used, this number being decided upon after three years of trial in using larger and smaller groups. This allows one student to be behind the screen for examination, two to be placed on a low bench in front of the screen, and four more on a second bench behind the first one. The instructor is behind the entire group. Since his visual acuity is cut down by his distance from the screen, his remarks will be more nearly within the range of understanding of the

students. Each student is kept under observation for a short time and then replaced, so that one student sees the thorax of six others. No attempt is made to point out all the features on any one case, the most obvious points only being commented upon. In one student, costal respiration will be marked; in another, interesting slopes of the clavicles, while in a third, the influence of the movements of the diaphragm upon the heart may be marked.

At appropriate times, further demonstrations are given: at Cincinnati, we gave a total of seven. For the digestive tract, two sets of demonstrations are employed, one occurring when a study of the tract is begun, to show the position of the viscera in the living (for it is folly to allow the student to learn a set of relations from the text-book, only to tell him a few days later that it is all wrong). The other demonstration is given as the study nears completion, to show the outlines of structures and, more especially, to show motility. Orthodiagrams are made and these are copied full size so that each student has his personal one when the surface anatomy of the thorax and abdomen is studied. These orthodiagrams are mounted in the laboratory, arranged in order according to constitutional type, so that they may be observed by all. With a skin pencil, the outlines of these orthodiagrams are traced on the skin of the student. The fundamental observations of Dr. R. Walter Mills on habitus are brought before the students, as well as the recent work in this field. These procedures complete the correlating of the dissection with the living. In many laboratories of anatomy and physiology, since the time of Sir Charles Bell, the outlines of organs have been drawn upon the skins of students, but these have always been the outlines of dead organs on the skins of living students. If it were not for the ultra-specialisms in medical education in the present time, physical diagnosis could be taught to advantage here, too. As it is, surface anatomy is limited to inspection and to palpation of the skeletal prominences, leaving the refinements of palpation, with percussion and auscultation, to the Department of Physical Diagnosis.

By the end of the course, the student's knowledge of how to look at the film is an advantage to him in studying even the more or less fixed parts of the body, parts which can be studied readily by other means. This is seen in the tracings made by students from the skull films. I am sure that these students have a better start in their profession than those to whom anatomy is taught without the roentgen laboratory. This holds true, no matter what type of course has been presented. The introduction of the roentgen laboratory need not alter the general method of teaching. The spirit of the laboratory has always depended upon the instructor in charge. Initiative, independence, and habits of observation are as readily inculcated about a film or fluoroscopic screen as about the dissecting table.

The anatomist finds that the roentgen ray frequently gives information in a short time which otherwise could be acquired only laboriously. Omitting from the discussion the more obvious field of the relations and physiology of the digestive tract, we may enumerate a few of the types of investigation which have been followed. The development of the skeletal system, which takes place during childhood and early adult life, at a time when it is hardest to obtain anatomic material for study, would be practically barren were it not for the many thousands of films made of the growing skeletal system. The roentgen ray, moreover, enables one to obtain the equivalent of skeletons of the same individual at different ages. Any of us, in a relatively short time and at no great expense, can develop a collection of films showing the development of the skeleton, that, for content, would put to shame the skeletal material of old, established museums. The various ducts and tubular structures of the body, even should they be unsuited for study in the

living by the roentgen method, can be studied conveniently on anatomic specimens.

The practitioners of certain of the specialties, particularly of ophthalmology and otolaryngology, may not think of themselves as being anatomists, but they are, nevertheless, for they make extensive observations on variations. When they refer a patient to a roentgenologist for examination, the roentgenologist can report upon pathologic changes found; but, in addition, it is certainly within his province as a consultant to indicate the anatomy as found in the living in the particular case at hand. Certainly in the skull the individual variation is so great that, except for the broadest generalizations, the text-book descriptions are inadequate.

The roentgenologist can make daily use of the rich anatomic and anthropologic material found in the libraries of books and specimens. The large body of known facts about the peculiarities of the ossification of the skull in the various races is particularly significant in the mixed population which we have in America. The knowledge of accidents of development, such as the persistence or disappearance of sutures and fontanelles, is of daily value. If the roentgenologist is to act as an anatomic consultant as indicated above, he must be familiar with the structures, not only as he sees them in two dimensions, but in the three dimensions in which the other specialists view the parts. The aid which anatomy can render to roentgenology is, however, not all in the past tense and, therefore, already available in books or in collections of specimens. There are many problems, particularly in the head, neck, and chest, which are yet to be worked out. The field of vascular anomalies has been incompletely studied. Up to this time anomalous vessels have been discovered on the roentgen film by the location of shadows which were cleared up later by autopsy findings. I am proposing that the known variations in the great vascular trunks be restudied, this time not from the standpoint of embryologic development but from the standpoint of their contours and particularly their outlines as they would appear in silhouette. For example, I think that I am able to recognize a left superior vena cava in the roentgen films because of silhouette studies made of this rather unusual anomaly on the anatomic specimen. In other words, I am proposing that we reverse the common method of finding a shadow, then looking for its explanation. Instead, we shall endeavor to find out the sorts of shadows which may be expected from the occasionaly occurring variations which come to light, or have come to light, in the laboratories of anatomy and pathology.

It must be remembered that in America, at least, the roentgenologist will be compelled to study bone pathology in the anatomic laboratory. With the incompleteness of postmortem examinations which popular opinion makes necessary, it is practically impossible to obtain specimens of the long bones or of the bones of the face for gross or microscopic study of pathologic change.

Furthermore, the roentgenologist will find a large group of young adults as students in the anatomical laboratory and he will find that they will willingly cooperate by furnishing themselves as subjects in obtaining series of normal films. Here it should be pointed out that films obtained from any group of individuals not presenting symptoms are of more value than the so-called normal films which the roentgenologist culls from his files. The subject of the film in the roentgenologist's laboratory was undoubtedly presenting some symptoms, and, while there may be no gross change detectable, there may be present changes of tone and minor changes of structure which would prevent them from being classed as strictly normal.

In conclusion, I hope that I have shown you that, while the study and teaching of anatomy have more to gain in the approach to their problems of the structure and gross function of the living from the technics of roentgenology than from any

other method, this important aid must be presented in a systematic and well-thought-out manner to be most effective. As for the correlation of anatomy and roentgenology for those who profess these disciplines, the greatest number of problems will be worked out with the anatomist seeing the body through the film or screen of the roentgenologist and the roentgenologist visualizing or feeling the third dimension with the sensorium of the anatomist. The ideal situation will probably be realized when the anatomist and roentgenologist are intimate confrères and when everywhere there are radiologic as well as dissecting facilities in the anatomical laboratory, and when there is as large a reference library of anatomical specimens in the roentgen laboratory as opportunity will permit.

DIFFUSE INTERSTITIAL CALCINOSIS[1]

REPORT OF A CASE, WITH A REVIEW OF THE LITERATURE

By THOMAS SCHOLZ, M.D., *New York*

THE name "interstitial calcinosis" was introduced and the condition defined as a nosological entity by Krause, in 1909.

The disease is anatomically characterized by inflammatory changes in the interstitial connective tissue of the muscles and the subcutaneous region, with secondary calcium deposits confined to the fibrous elements. It may occur in either a localized or a diffuse form. As the condition is rare and especially in view of the fact that postmortem studies have been made in only three instances, it may be of interest to report an additional case, with autopsy findings.

The case to be reported was observed by me some years ago in the roentgen department of the Montefiore Home. Its findings were brought into recollection recently in connection with the preparation of a paper on calcification in scleroderma, on account of the great similarity in the roentgenologic appearance of these two conditions.

Prior to her admission to the Montefiore Home the patient had been in the Mt. Sinai Hospital, where the diagnosis of calcinosis was made clinically by Dr. Sara Welt, and radiographically by Dr. Leopold Jaches. It is with a feeling of deep appreciation that advantage is being taken by me of the permission kindly granted by both Dr. Welt and Dr. Jaches to publish the case first.

REPORT OF CASE

F. M., 11 years of age, was admitted to the Montefiore Home on Dec. 27, 1916.

Family History.—Mother had died of diabetes two years previously. Father, a brother, and a sister alive and well.

Past Personal History.—She had had measles and scarlet fever in early childhood, from which she apparently recovered completely. She felt well until the onset of the illness about to be reported.

Present Illness.—Sixteen months before, without any undue exposure to cold or other apparent cause, she experienced a sudden attack of pain in both legs. This attack lasted approximately three weeks, after which it gradually disappeared. While it lasted, the pain was constant, but varied greatly in intensity, being worse during the night. It did not involve the knees, which showed free motion. There was no swelling, discoloration, or any change in the appearance of the skin. Appetite, bowels, and urination were normal. The sleep was disturbed on account of the pain.

Three months later the pain recurred, this time involving all the extremities and being associated with diffuse swelling. However, the joints again were free. A week later swelling of the neck ensued, with a slight rise in temperature. There was no dyspnea, precordial pain, sore throat, or other symptoms save the above. A few weeks later, approximately *six months after the onset of the disease, there appeared in both lower extremities small hard nodules* which could be palpated through the skin. These nodules were not tender.

During the following months the skin of the extremities, and, to a lesser degree, also of the neck and face, became edematous and presented in many places a reddish discoloration. This gradually disappeared and the skin became dry, scaly, and tense, showing patches of brownish discoloration. There was a feeling of tightness all over the body. Evidently due to the tenseness of the skin and its apparent loss of elasticity, the movements of the joints of the extremities, neck, and maxillæ

[1] Demonstrated before the New York Physicians Association, Feb. 4, 1919.

became impaired, so that there developed difficulty with walking and mastication. Hard nodules appeared also in the upper extremities and around the neck and increased in number. A moderate loss in weight began to take place.

Status on Admission.—The patient is a poorly nourished girl, presenting a somewhat mask-like facial expression. The skin of the entire body, including the scalp, is dry and scaly. It is tense, without elasticity, fixed to the subjacent tissues, and shows a brownish discoloration. Over the distal parts of the lower extremities the color is bluish, intermingled with occasional small reddish patches of irregular form. All over the body, but especially on the face and upper part of neck, there are numerous small, fine, flat scars of bluish, reddish, or white color, varying in size from that of a grain of wheat to that of a grain of corn. Over both internal condyles there are decubitus ulcers. There is swelling of the cervical, but not of the axillary or popliteal, glands. Over the occipital region is seen a bald spot, evidently due to pressure.

Palpation shows evidence of atrophy affecting all muscle groups, but especially the extensors of the knees. A number of small, hard, non-tender nodules are felt through the skin of the extremities, buttocks, and neck. Some of them are immediately underneath the skin and even appear to project through it.

Motion in most of the joints, especially in those of the extremities, is limited, evidently due to tenseness of the skin and contractures of muscles. The jaws cannot be opened beyond one inch. This, also, is due to contractures of the muscles, as the articulation itself appears to be free. The flexor tendons at the knees are prominent, with extension greatly limited. Attempts at full extension are painful, so that some of the joints, especially the knees, are automatically kept in semiflexed position. The joints themselves are free. There is no tremor or ataxia, no pain or tenderness on palpation.

Examinations of the eyes, ears, throat, tongue, nose, lungs, and heart are negative. Reflexes are normal.

Fig. 1. Calcium deposits in the left upper extremity.

The urine showed a few hyaline and granular casts. Red blood cells were 4,000,000; white cells, 10,000. Blood pressure was 100/70. The Wassermann test was negative.

Further Course of the Disease.—For about a year the condition remained quite stationary. The patient walked little, and that with great difficulty. Gradually, however, the tenseness of the skin became more marked and the contractures of the muscles increased, so that finally, about six months prior to her death, the patient became permanently bedridden. To avoid discomfort she lay in a semiflexed posture, with the legs drawn up and acutely flexed upon the abdomen.

Later, pain developed which evidently was due to the increase in the various muscle contractures. Gradually the sub-

Fig. 2. Calcium deposits in the right upper extremity.

cutaneous nodules also increased in number and now became painful. Decubitus ulcers developed over the buttocks. Breathing became shallow, evidently due to an increasing tightness of the skin, tachycardia grew pronounced, and evidence of pulmonary involvement set in. The patient's discomfort rapidly increased. For a few days before death she was in extreme pain. She succumbed finally to a sudden pharyngeal spasm during an attempt to swallow food.

Duration of the disease: two years and ten months.

Roentgen Examination (*Dec. 29, 1916*).—Radiography of the entire muscular system revealed extensive calcium deposits throughout the soft tissues of all the extremities, most in evidence in the thighs, legs, upper arms, and forearms, while hands, feet, and hips presented only an occasional solitary small patch. Few small calcified areas were found in the soft tissues of the trunk and neck, while the soft parts of the head revealed none. Most of the deposits in the extremities were confluent, presenting longitudinally arranged patches. Isolated deposits ranged from pinhead size to small clusters of various sizes and shapes. Plates taken at different angles revealed that the calcified areas were situated on various horizontal levels of the soft parts and that they had no connection with the bones. Measurements also showed that the calcifying process was most pronounced just below the subcutaneous region (Figs. 1–4).

The lungs presented a few infiltrative spots within the apices, especially the left. The diaphragmatic excursions were shallow and rapid. The heart was moderately hypertrophic. The aorta appeared normal.

The genito-urinary tract failed to present any demonstrable abnormality.

The stomach was dropped, elongated, and very atonic. Peristalsis was greatly diminished. There was a marked gastric residue after six hours. The small intestine showed no abnormality. The colon was ptosed and presented pronounced stagnation.

The bony system revealed no abnormality as to size, shape, or epiphyseal development. The existing diffuse bone atrophy was such as could be satisfactorily explained on the basis of inactivity.

The further course of the patient's condition was checked up by repeated x-ray examinations, which failed, however, to reveal any additional information except that the number of calcified areas appeared to increase slightly and that definite evidence of a left apical tuberculosis, with pleural involvement, developed.

Postmortem Findings.—Grossly it was found that the calcifying process in the extremities was most pronounced in the superficial muscular layers. In many places there were small cyst-like cavities containing degenerated fibrous tissue impregnated with calcium salts. The muscles in the calcified areas showed a marked increase in fibrous tissue and petechial hemorrhages appeared throughout the muscle structure.

Microscopic examination revealed an increase in the connective tissue not only of the septal, but also of the interfibrillar elements. These connective tissue bundles appeared in many places four or five times normal size and seemed to press apart the muscle fibers. There was infiltration of the interstitial tissue with small round cells. The muscle fibers in places presented a good amount of striation: the number of their nuclei was increased and sometimes arranged in long lines. In other places the individual muscle fibers appeared markedly shortened and on cross-section their diameter was often seen to be either enlarged or diminished. The striation was almost entirely absent and round-cell infiltration was seen to invade the muscle fibers. The increased connective tissue appeared hard and crude, with less round-cell infiltration.

In the skin the blood vessels were markedly thickened. In many places the epithelial layers were absent, having been replaced by connective tissue.

The calcium, which consisted of 75 per cent calcium phosphate and 25 per cent calcium carbonate, was deposited in form of very fine corns along the connective tissue fibrils. These calcium deposits were strictly confined to the interstitial tissues, not involving the muscles, no matter what degree of degeneration the latter presented. In the tendinous portions of the muscles, also, the calcification was confined to the enclosing fibrous sheaths.

In a number of places the calcium deposits were arranged in the form of clusters situated in cavities. Some of these minute cavities were found in the deeper layers of the corium and in the subcutaneous fat tissue, and were surrounded by hard fibrous tissue, poor in cellular elements. In some instances the inside of the cavity was divided by connective tissue strands. These calcified changes, when involving the fat tissue, gave a picture quite different from that usually presented by fat necrosis with secondary calcification. Similar clusters of calcium deposits within small cavities were found in the deeper muscular layers.

Fig. 3. Calcium deposits in the left lower extremity.

Outside of the above anatomical findings there was evidence of an advanced left apical tuberculosis, with bronchopneumonia and pleural adhesions. The mesenterial glands contained no calcium deposits. The thyroid gland was not enlarged nor did it present any macroscopic changes on cross-section.

Fig. 4. Calcium deposits in the right lower extremity.

REVIEW OF LITERATURE

As the cases belonging to the group of interstitial calcinosis have been published in the vast majority of instances under various names, the perusal of the literature was somewhat difficult. The case histories are fairly typical, and the reader is referred to the appended bibliography.

CASES ERRONEOUSLY CLASSIFIED BY SOME WRITERS AS BELONGING TO THIS GROUP

Meyer's (27) patient was a man of 45 whose leg was amputated for chronic suppurative gangrene. The author found in the specimen extensive "ossification of the muscles and tendons." A study of the article makes it evident that the case was one of chronic osteomyelitis with secondary calcification.

Milian (28) described, in 1899, the case of a girl, 8 years of age, in whom (evidently secondary to a trauma) there developed an abscess in the plantar region of the left foot. Incision of the abscess released greasy pus. The patient had been and remained otherwise perfectly healthy and presented none of the characteristics of interstitial calcinosis.

Beck (1) reported, in 1901, the case of a man, 42 years old, who first had had an inflammatory condition of the right big toe which necessitated amputation. The specimen showed calcium deposits. Two years later a fluctuating tumor appeared on the dorsum of the left hand. Operation revealed extensive destruction of the soft and bony parts, associated with calcification within the soft tissues, especially the tendons. This case, also, fails to present any of the other features typical of our group.

Wolff's (48) patient was a man of 62 in whom there developed in the right thigh a large abscess which opened spontaneously and discharged a great amount of greasy pus. Subsequent operation revealed calcium deposits in the tendon of the semi-tendinosus muscle. Radiographic examination showed the presence of similar calcium deposits in the left thigh. In view of the co-existence of extensive calcification of the arteries and the absence of any other characteristics of our group, it is fair to explain the findings in this case on an arteriosclerotic basis.

CLINICAL MANIFESTATIONS

The most outstanding clinical feature of the condition termed by Krause "interstitial calcinosis" is the appearance of small hard subcutaneous nodules which have the tendency to open spontaneously and to discharge greasy pus, leaving slowly healing ulcers. These nodules may make their

first appearance in any part of the body, but usually in the extremities, especially the lower, in the buttocks, and in the neck. From the initial sites they may either spread over large areas and even over the entire body, as a rule symmetrically, or they may remain localized. They are usually at first not painful or tender, but may become so later. They remain small, only rarely increasing slightly in size. The appearance of the nodules is as a rule preceded, less frequently followed, by cutaneous changes, the skin becoming first swollen and red, later dry, indurated, glossy, and tense, showing usually brownish, rarely bluish, discoloration and often also small whitish scars.

In the *diffuse form*, which is by far the more common type, there develop later muscle atrophy and muscle contractures, especially in the flexure muscles. These, together with the tense skin, cause an increasing ankylosis of the joints. Thus we obtain in the fully developed and advanced stages the picture of a patient unable to walk, finding most comfort in a semi-flexed posture. Mastication is interfered with; the breathing is shallow and rapid; the face has a mask-like appearance; bed sores develop; with increasing muscle contractures, pain becomes acute and permanent; the nodules increase in numbers and become acutely tender, emaciation is progressive, and finally, all these signs and symptoms indicate the stage which leads to exitus. Pulmonary tuberculosis or aspiration pneumonia is apt to develop in the final stage and may prove the immediate cause of death.

The onset is sometimes most insidious, so that the appearance of the subcutaneous nodules may be the first noticeable sign. In other instances the first evidence is the formation of an abscess which either spontaneously or on incision discharges greasy pus. In still other cases the patient complains first of a sense of fatigue in the extremities, without any objective evidence. Rarely does the disease show an acute onset, with sudden swelling and reddening of the skin.

Its course is slow and characterized by intermissions and remissions. Gradually, however, sometimes over a period of many years, a downward progress of the condition can be noticed.

The *localized form*, much less common, may involve any part of the body, but preferably the fingers and toes. In contrast to the diffuse form, its onset usually is acute, with swelling and reddening of the skin, to be followed later by the appearance of subcutaneous nodules. Its course, also, is characterized by intermissions and remissions. It rarely leads to deformities, but remains on the whole stationary and does not vitally interfere with the patient's general health. Here, too, the skin usually assumes later a dry, tense, scaly, brownish appearance, and the nodules have a tendency to break down and to discharge greasy pus.

The prognosis is bad in the diffuse form, good *quoad vitam* in the localized form. A complete recovery has not been reported yet in either type.

In its diffuse form, the disease usually begins in the first or second decade, rarely later. The localized form occurs in persons of middle or even advanced age. Females are more susceptible to it than males.

CLINICAL DIFFERENTIAL DIAGNOSIS

The palpable subcutaneous nodules, with their tendency to break up spontaneously and to discharge greasy pus, definitely settle the diagnosis of interstitial calcinosis. Differential diagnostic considerations, therefore, are applicable only to the prenodular stages of the disease during which the clinical picture as a rule is dominated by skin changes. As the latter may represent any degree, ranging from the edematous to the most advanced atrophic stage and may involve to any extent and in any form practically any part of the body, we have to keep in mind, for local differentiation at least, all those conditions which are associated with the same or similar cutaneous findings, namely,

scleroderma, dermatomyositis, scleredema melorheostosis, Meige's trophoedéme, and myxedema.

The differentiation from myxedema is self-evident on the basis of the other clinical data. The analogy with melorheostosis, a condition first described by Leri and Joanny (22) and characterized by a flowing hyperostosis of one single limb, may appear far-fetched. However, it will not be found to be so if we remember that in this disease there may occur, as pointed out by Meisels (26), symmetrically arranged extensive skin changes consisting of induration, glossy and tense appearance, and occasionally bluish or brownish discoloration. The differentiation is made roentgenologically as explained below.

The distinction from scleredema adultorum, a condition first described by Buschke (5) and recently exhaustively reviewed by Epstein (12), may prove for a long period of time difficult or even impossible until the diagnosis is decided by the appearance of the subcutaneous nodules in favor of calcinosis, or by the complete disappearance of the skin changes in favor of scleredema. The cutaneous changes in calcinosis are permanent: calcification never takes place in scleredema.

In Meige's trophoedéme there is a tendency toward elephantiasis and the condition often is associated with spina bifida occulta so that radiography may prove of differential diagnostic value.

Dermatomyositis and scleroderma may produce exactly the same clinical picture as interstitial calcinosis, so that a definite differentiation may be and often is absolutely impossible until the appearance of the subcutaneous nodules; and even then a distinction from scleroderma may be very difficult because, in the latter condition also may occasionally be noted small superficial nodules which may break up and discharge greasy pus.

ETIOLOGY

As etiologic factors are mentioned cold, trauma, rheumatism, tuberculosis, parasitic infection of unknown origin, etc. In a large percentage of instances, however, it is stated that the condition started without any apparent cause; yet, in studying the case histories the reader is impressed by one fact which has not been thus far mentioned by any writer on the subject, namely, that all the patients belong to the poorer class, living, in most instances, under poor hygienic and inadequate nutritional conditions. Besides, in some cases other chronic conditions like tuberculosis or rickets, contributed to weakening the patient's state of health. It seems to me, therefore, that in this disease a *lowered vitality of the tissues is the predisposing factor*, and that with this as a basis some additional *causa nocens*, either in form of a cold or a trauma, may act as the direct cause of the disease. That trauma plays a rôle is strikingly shown by the cases of Duret, Jeanne, Dietschy, Morse, and Friedländer, while those of Neuwirth and Krause are examples of the theory of cold.

ROENTGEN-RAY FINDINGS

The x-ray findings are characterized by the usual shadows suggestive of calcification, the size and shape of these shadows depending upon the stage of the disease. In comparatively early cases, like that of Morse, the shadows are small and present no definite arrangement. Later, with the increase in the calcification, they become larger, may coalesce, and assume the form of plaques which present a longitudinal arrangement. Some of them may attain a massive appearance, especially around the large joints.

In the diffuse form, the calcium shadows are distributed mainly throughout the legs, thighs, forearms, and upper arms, rarely—and then usually to a much lesser degree—throughout the hands, feet, trunk, and face. Calcification within the abdominal wall is best shown by means of lateral views. Calcium deposits within the mesenteric glands, as found on autopsy in the cases of Tilp and of Versé, may be

expected to be visualized radiographically *intra vitam*. The roentgenograms of the specimen in Versé's case showed characteristic ring-like shadows.

The calcium shadows are not confined to the areas of the palpable subcutaneous nodules, but are diffusely scattered also outside of the tumors. By means of plates taken at various angles it can be shown that the calcified spots are situated on various levels of depth, extending from the subcutaneous region down to the deepest muscle layers. The shadows have no connection with the bony parts.

It is of great interest to note that calcified spots may be found radiographically in regions over which the skin may appear perfectly normal; and, on the other hand, no calcium deposits may be found in areas over which the skin presents most advanced changes. It is, therefore, advisable in this type of case always to x-ray the entire body. Such systematical complete radiographic surveys are, for obvious reasons, a far better means of widening our knowledge as to the occurrence and distribution of these calcium deposits than postmortem examinations.

It may also be of great importance for the sake of the therapeutic results to order x-ray examinations in the early stage of the disease. One may thus occasionally succeed in arriving at a correct diagnosis long before the appearance of the subcutaneous nodules or even before the beginning of atrophic skin changes, whereby therapeutic measures may be at once begun.

The bones present no abnormality except for a moderate degree of atrophy, nor are there any bony arthritic changes.

ROENTGENOLOGICAL DIFFERENTIAL DIAGNOSIS

In regard to roentgenologic differential diagnosis there have to be considered mainly scleroderma, to a lesser degree also hemangioma and melorheostosis. The differentiation between calcinosis and scleroderma, as described by me recently (40), is impossible except, perhaps, with the aid of the clinical data. Calcification in hemangioma, as reported by Ruggles (37), Johnson (18) and others, may be definitely distinguished from calcinosis by its characteristic small, round, concentric, calcified bodies. In melorheostosis there may occur massive calcium deposits around the large joints of the involved limb. These calcified areas, as described, for instance, by Meisels (26) around the right hip, and by Kraft (19) at the left shoulder, may remind one of the calcifying process in our cases. However, the co-existing characteristic bony changes make a differentiation easy, and the readiness with which interstitial calcinosis is distinguished roentgenologically from myositis ossificans is self-evident. Since calcium deposits in abscesses are not very rare, such radiographic findings are distinguished from calcinosis by the fact that they are confined to the abscess area.

PATHOLOGY

The anatomical picture is characterized by a marked hypertrophy of the interstitial connective tissue, with calcium deposits within the latter. The small, hard, subcutaneous nodules which are felt on palpation are produced by clusters of calcium deposits within bundles of hypertrophied fibrous tissue. There is also, however, as shown by the x-rays, calcification outside of the nodules, the latter being situated not only immediately underneath the skin, but also in the deeper soft tissue layers, entirely outside of the reach of external palpation. The number of palpable nodules, therefore, is no reliable indicator for the extent of the calcifying process. With the connective tissue hypertrophy is associated a diffuse myositis at various stages; however, there also may be found large areas of myositis without connective tissue changes.

The calcification process is confined strictly to the fibrous tissue, and here only to those fibers which have undergone a certain

amount of degeneration. Muscle fibers, no matter how degenerated they may be, contain no calcium salts.

The calcium is deposited in form of fine glistening grains along the connective tissue fibrils, and sometimes it is seen in small vacuoles filled with degenerated fibrous tissue. Toward the skin, the hypertrophied fibrous tissue is seen destroying and replacing the subcutaneous fat. In bioptic examinations, in which the removed specimen, for obvious reasons, is obtained from a comparatively superficial layer, this fibrous degeneration of the subcutaneous fat may be and has been mistaken for fat necrosis. This is similar to that found in the abdominal cavity in acute pancreatitis in cases in which the lesion is due to lipolytic ferment, so that the presence of such a ferment in the subcutaneous tissue has been assumed. This, of course, is not so. The subcutaneous changes in calcinosis have nothing to do with what usually is understood by fat necrosis. In our cases the process is a mechanical crowding out, destruction and replacement of the fat by the hypertrophied connective tissue extending from below. In the skin, the blood vessels are markedly thickened and in many places the epithelial layer is replaced by connective tissue.

Calcium salts may also be found deposited in the mesenteric glands. Here, too, the calcification process involves not the glandular, but only the connective tissue, elements. Enlargement of the thyroid has occasionally been reported.

There are no pathologic bony changes, the moderate amount of diffuse atrophy encountered in advanced cases of long standing being due to inactivity.

COMMENT

Though the cases grouped under the term "interstitial calcinosis" evidently present a characteristic clinical and pathologic picture, yet there exists a noticeable divergence of opinion in regard to the nature of the disease. While some authors, as, for instance, Krause (21), Versé (43), and most of the French authors, consider it a separate clinical and pathologic entity, others believe it to be only one phase of a long-continued inflammatory process common also to certain other diseases. Thus Oehme (33) is of the opinion that the name "interstitial calcinosis" merely indicates one single diagnostic point occurring evidently in the last stage of the disease. He, therefore, suggests "universal sclerosis of the connective tissue" as a more appropriate name for the disease, which latter he places among the large group of sclerodermas.

There is no doubt but that the calcification process in our cases is only one incident of an advanced stage of a chronic condition, which otherwise presents a surprising similarity with cutaneous changes occurring in various other diseases. This similarity is at times so striking that one cannot help assuming that some of these diseases probably are only various degrees of one and the same pathologic process. The interrelationship between these various types of cutaneous manifestations, about which we know little yet, would possibly be better understood if, instead of classifying them as separate clinical and pathologic entities, we would group them under one term like "cutaneous sclerodema" and then study the analogous and divergent features of each. Such a comparative study will reveal, as is being suspected by various authors, that there is not only a clinical, but to a certain extent also a pathologic-anatomical similarity between some of these cases. Connective tissue hypertrophy, for instance, is found in all of them, but in varying degrees. The original factors causing interference with the blood and lymph supply of the skin may in some instances be of a physiochemical nature, correction of which may bring about a complete *restitutio ad integrum* as observed in scleredema adultorum. In other cases the basal cause may be mainly of endocrinologic character, while

in still others, the basal lesion is of a purely anatomic type. In interstitial calcinosis it is, according to our present autopsy experience, quite certain that the condition begins with a myositis, accompanied or followed by a connective tissue hypertrophy. As the latter gradually invades the subcutaneous region, skin changes begin to appear. The period of the appearance of cutaneous changes depends, therefore, upon the rapidity with which the fibrotic process reaches the region of the skin. The hypertrophied connective tissue then undergoes retrogressive changes which are followed by the deposition of calcium salts in the degenerated fibrous elements.

In regard to the nature of the calcifying process in these cases a certain amount of understanding may be obtained by a brief consideration of the problem of calcification.

As pointed out on previous occasions (38, 39), it is well to accept the usual classification of calcification into the metastatic and dystrophic forms.

The metastatic calcification, as first described by Virchow (45), then by Hofmeister (15), Versé (43), Wells (46) and others, is characterized by an over-saturation of the blood with calcium salts secondary to some extensive bone destructive process like chronic myelogenous leukemia, osteomalacia, bone destructive tumors, etc., in association with a co-existing nephritis, followed by calcium deposits in *healthy* tissue, namely, the lung, gastric mucosa, kidneys, arteries, and heart. This phenomenon is explained on the basis that in those organs acids are excreted into cavities which leave the fluids in the substances of these parts correspondingly alkaline. This increase in the alkalinity of the fluids makes the calcium salts decidedly less soluble, so that, in instances in which for some reasons the total amount of free calcium salts in the body fluids is greatly increased and its prompt excretion interfered with, calcium may be deposited in these organs. What other factors may enter into the causation of this type of calcification is not quite understood yet. Hueper (16) has succeeded in producing metastatic calcification in the above-mentioned organs in dogs after injection of parathyroid extract.

The metastatic calcification is also of roentgenologic interest. One should remember that it never occurs in muscular or cutaneous tissue, so that calcium deposits in these regions should never be explained by the roentgenologist on a metastatic basis. Furthermore, the calcium deposits in the lung, stomach, kidneys, and heart may assume, as evidenced by the published autopsy reports, such large proportions that they can be noted macroscopically and even easily palpated in the specimen. It is, therefore, fair to assume that, though they have not yet been demonstrated radiographically *intra vitam*, these calcium deposits can be visualized by the x-rays, so that it would be advisable to make a special roentgenologic search for them in suitable cases.

All other types of calcification belong to the large dystrophic group in which a previous retrogressive change of the tissue in question is a *conditio sine qua non*. These degenerative changes may consist of retrogression taking place in the normal involution process of certain parts of the body. A typical example of it was shown by us (2) to be the pineal body. Other dystrophic calcifications are so commonly observed in roentgenologic work that one rarely stops to think of their causes, and it is only in instances of an unusual location or extent of the process that our interest in this subject is aroused. In going, then, into this question one is astounded by the immense amount of work done in this respect and the large number of theories established. Since it would lead too far even to touch lightly upon this question, I will confine myself to the report of a personal observation made in connection with my roentgenologic postmortem studies during the years 1915 to 1920 in the Montefiore Home, where the chronic material was ideal for such purposes.

During microscopic studies of calcified areas of a great variety of organs I was impressed by the uniformly observed presence of degenerated fibrous tissue in the region of the calcium deposits. Following the microscopic observations in our case of interstitial calcinosis, in which the location of calcium was definitely established to be in degenerated fibrous tissue only, the old slides of various types of calcification were studied again and observations in new material were added. As a result of these studies (to be described in a separate paper), I came to the conclusion that in the dystrophic type of calcification the calcium is deposited only in pathologically changed fibrous tissue, and that other tissue elements, no matter in what stage of degeneration they may be, never become the seat of the calcium deposits. This conclusion appears to be supported by the investigation of Mays (25). It would also explain the deposition of calcium salts in conditions which are characterized by an extensive pathologic fibrosis, as, for instance, in hemangioma, osteoplastic carcinoma, etc. In other words, it seems that *pathologic fibrous tissue is the sole carrier of the calcium salts in any kind of pathologic calcification*, except for the metastatic form.

That outside of the fibrous degeneration there must be still other factors playing a rôle in calcification is obvious. Investigations in regard to calcium metabolism have failed to yield uniform conclusions, probably owing to the difficulty of checking up properly the intake and excretion of the calcium salts. Thus, Copp (6) found retention of calcium in hypertrophic arthritis and loss of calcium in atrophic osteo-arthritis, while Friedländer's (13) observations of the calcium metabolism in his case of advanced interstitial calcinosis revealed normal figures. Nor is it definitely established what influence disturbances of the parathyroids have upon the calcium metabolism. Of interest in this respect are the investigations of Bulger and Barr (4), who proved that changes in the function of the parathyroids may, but not always do, influence the level of the serum calcium.

The decisive factors for the occurrence or non-occurrence of calcium salts in anatomically equally well suitable tissues probably are of still unknown intra-cellular nature. A new ray of hope for the final solution of the general problem of the deposition of calcium salts in the body was furnished recently by the investigations of Roseberry, Hastings, and Morse (36), who tried to determine whether or not the calcium salts of bone exist in crystalline form and what this crystalline form is. They have shown by means of x-ray spectrograms of bone that the latter has a crystalline structure and that this structure conforms most closely to that of dahllite, a carbonate-phosphate. These findings were confirmed by the work of Bogert and Hastings (3), who came to the conclusion that the chief inorganic constituent of bones seems to be neither tertiary calcium phosphate nor calcium carbonate, but a crystalline salt containing carbonate, phosphate, and calcium in definite space relation with one another.

CONCLUSIONS

1. Interstitial calcinosis is clinically characterized by small, hard, subcutaneous nodules which show a tendency to open spontaneously and to discharge greasy pus, leaving slowly healing ulcers. It may occur in a localized form, involving practically any part of the body, or a diffuse form, which may gradually extend over the entire body. The appearance of the nodules may be preceded or followed by scleroderma-like cutaneous changes which may become an outstanding clinical feature.

2. Roentgenologically it presents characteristic evidence of calcification. The latter is most common in the extremities.

3. Pathologically the condition is characterized by hypertrophy and degeneration of the interstitial connective tissue, with secondary deposition of calcium salts in the fibrous tissue elements.

4. Notwithstanding its characteristic clinical, roentgenologic, and pathologic findings, the condition probably is not to be classified as a separate clinical and pathologic entity, but as an advanced stage of a chronic inflammatory condition which may be the basic lesion common to all the members of the scleroderma group.

5. Autopsy evidence shows that in interstitial calcinosis the calcium salts are deposited only in degenerated fibrous tissue, and that muscle fibers, no matter how degenerated they may be, do not contain any calcium. This tends to support the theory that in the dystrophic type of calcification pathologic connective tissue is the sole carrier of the deposited calcium salts.

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THE ROENTGEN-RAY TREATMENT OF INOPERABLE CARCINOMA OF THE BREAST BY THE METHOD OF MULTIPLE CONVERGING BEAMS[1]

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IN this paper, the term "inoperable carcinoma," applying throughout to carcinoma of the breast, will include ulcerated carcinoma, carcinoma fixed to the thoracic wall, carcinoma with widespread cutaneous metastatis, carcinoma which could be extirpated surgically but accompanied by involvement of supraclavicular nodes, carcinoma with extensive involvement of axillary and supraclavicular nodes, carcinoma with osseous or visceral metastasis irrespective of nodal involvement, and carcinoma in the presence of such poor physical condition, due to complicating organic disease, that the risk of operation would be too great. The study concerns 41 patients treated in the Section on Therapeutic Radiology at the Mayo Clinic in the years 1925 to 1929, inclusive.

Obviously, treatment in advanced stages of carcinoma of this type has little to offer in the way of cure. For this reason, radical surgical and radiologic treatments are not justified, even though they may give brilliant and unexpected results in a small percentage of cases. Treatment, therefore, is palliative only, and consists of measures to relieve discomfort from the tumor, to check its dissemination, to postpone or prevent fungation, to make fungation more tolerable if it already has taken place, and to maintain the patient in as good general physical condition as is possible until death ensues from visceral metastasis. Such treatment may consist of various measures, among which radiologic methods designed to hold the carcinoma in abeyance have a place. At the Mayo Clinic, such methods have produced results superior to those of all other methods investigated.

Carcinoma of the breast may occur at any age and in persons of either sex. Of this group, three of the patients were between 20 and 30 years of age, five between 31 and 40, four between 41 and 50, eighteen between 51 and 60, seven between 61 and 70, and four were more than 70 years of age. In 19 cases the tumor was of the right breast; in 20, of the left breast and in two, bilateral. The group is too small to permit definite data to be obtained on the relationship of age to the virulence of the tumor, or to duration of the tumor. Three patients each had noticed a tumor in the breast from two to three months before they came to the Clinic; ten, from three to six months before; six, from six months to a year before; six, for thirteen months to one and one-half years before; five, for nineteen months to two years before; three, for two to three years before; five, for three to five years before, and three, for five to eight years before. With such wide variations in duration of carcinomas which had not received treatment, it is apparent that degrees of clinical malignancy varied widely, and that estimation of curative results or of degree of palliation, therefore, is difficult. However, since benefit from treatment and not cure was expected, the results of radiotherapy can, nevertheless, be determined on a purely objective basis.

Twelve of these 41 patients had axillary and supraclavicular metastasis, nine had ulcerated tumors with axillary involvement, five had ulcerated tumors and axillary and supraclavicular involvement, two had supraclavicular nodes in addition to the ulceration, two had such extensive involvement of the skin that radical operation was contra-indicated, the tumor of three was sufficiently fixed to the thoracic wall to preclude complete extirpation by operation, and of eight the complicating factors made the risk of operation excessive.

[1] Read before the meeting of the Chicago Roentgen Society, March 9, 1932.

Among these patients there was one case of "cancer *en cuirasse*," three cases of the inflammatory type of tumor, and one case of "rose cancer" (an inflammatory type of lesion).

The often-repeated statement that the condition of the breast has no relationship to the situation or extent of metastasis beyond the regional nodes was confirmed in investigation of this group. In 39 of the cases there was no evidence of metastasis to the structures in the thorax, and in two cases evidence of involvement of the lung or pleura was obtained by roentgenography. In five cases there was metastasis to the spinal column or pelvis, in one case to the skull, and in three cases to the ribs. In none had the tumor metastasized to the liver or abdominal nodes or to the bones of the arm or shoulder. The incidence of metastasis, therefore, corresponded in essentials to that reported in similar groups of breast carcinoma.

Because there was no need of it, in the great majority of cases the clinical diagnosis was not confirmed by biopsy, but of the three cases in which specimens were taken for biopsy adenocarcinoma graded 4 was found in two, and adenocarcinoma graded 3 in one.

With the facilities available in the Clinic, radiotherapy of carcinoma of the breast is best carried out with roentgen rays generated at moderate or high voltage, supplemented, if indicated, by surface applications of radium in the form of a pack, and by interstitial radiation by tubes or needles. However, because of the demand on the supply of radium, made by an increasing volume of favorable cases of other types, recent practice has tended to limit radiologic treatment of carcinoma of the breast at the Mayo Clinic to the use of roentgen rays. By a slow process of development the technics to be described have been evolved, and even though they are improvements on previous methods which have been used in the Clinic they are not standardized, but are modified and individualized to suit the peculiarities of the various cases.

In treating lesions of the type in question, attention must be devoted to the local tumor as well as to metastatic growths in the axillary and supraclavicular nodes. The latter may be treated by external cross-fire of heavily filtered short wave length roentgen rays, by technics employing moderate voltage, by radium packs, or by interstitial radiation, and will not be considered in greater detail at present.

It has been only with the recent development of dosimeters that comparison of the effectiveness of roentgen therapeutic technics has been possible. Prior to the development of standardized dosimeters without a "hardness error" the clinical efficiency of radiation of different qualities was a matter largely left to clinical empiricism; but now that ionization systems designed to measure clinical doses of roentgen rays are easily available in this country and abroad, it is possible for the first time, not only for the individual therapeutist to standardize his own technics, but also to compare his set-ups and results with those of others. By the use of these standardized dosimeters, it is to be hoped that the long-standing controversy over the parts played by quality and quantity in producing biologic effects will be settled. Even though there is some clinical and experimental work tending to demonstrate the superiority of gamma rays over roentgen rays, it rather seems to me, in view of the fact that either special tumors or special biologic test objects were used in these researches, that the conclusions drawn from them must be accepted with much reservation, and that further confirmation will be required before they can be adopted for treatment of carcinoma of the breast.

As has been indicated, radiotherapy of inoperable carcinoma of the breast has been carried out almost entirely with roentgen rays, at first with roentgen rays generated at 200 kilovolts, and heavily filtered according to the well-known technics of "deep therapy." Because of the clinical inefficiency and inexpediency of this technic, treatment has been limited

in recent years largely to the use of "moderate voltage technic." One purpose of this paper is to validate the exclusion of high voltage in the treatment of inoperable carcinoma of the breast.

Here are three set-ups; the one to the left employs high voltage and the other two, moderate voltage.

200 K.V. (max.) 5 ma. 50 cm. T.S.D. 0.75 mm. Cu plus 1 mm. Al filter	135 K.V. (max.) 5 ma. 40 cm. T.S.D. 4 mm. Al filter	135 K.V. (max.) 5 ma. 40 cm. T.S.D. 6 mm. Al filter
Fields 8 x 8 to 15 x 15 cm.	Fields as before	Fields as before

In each of these set-ups, in which the roentgen rays are generated by a mechanical rectifier activating an air-cooled Coolidge tube, and in which voltage is determined by the accepted method of 125 mm. spheres, we have ascertained our threshold erythema dose to be 560 r measured in air, irrespective of which technic is used. These determinations of the dose have been made by a Victoreen and a Mecapion dosimeter, and even though they agree well with the accepted value of erythema dosage, they are subject to the variations incident to the use of any biologic unit. However, up to the present we have no more absolute measure of clinical doses than the threshold erythema, and until some further refinement of clinical dosimetry makes it expedient, we can adopt for our unit 560 r measured in air; this produces a safe, although not uniformly intense, radiodermatitis of first degree. Barring evidence to the contrary, the assumption has been made that all patients who have received 560 r, measured by a dosimeter, have received uniform doses of roentgen rays. In our department all machines used for treatment have been checked repeatedly by standard dosimeters, and, when necessary, corrections have been made in the time of exposure. We have not used a constant check on each dose administered because of the inconvenience of doing so, but we have relied on standardizations made of the output of each new tube, which we have assumed to remain constant barring some obvious mechanical or electric breakdown. Clinical observation of the cutaneous and other biologic reactions in daily treatment of patients have seemed to justify reliance on clinical dosage rather than on physical dosage.

It is self-evident that the actual "dose" in the skin will vary with the varying component of secondary rays from fields of various sizes, but in determining clinical doses this factor has been neglected, since the accepted technic of placing the ionization chamber in air is relied on to eliminate the scattered radiation. The suggestion made by Weatherwax and the writer, of placing the center of the axis of the chamber at a distance corresponding to the target-skin distance in question, has been followed. Measurements by means of the paraffin block are in progress, but are not at present sufficiently well checked to allow a statement of the magnitude of changes in surface doses produced by triangular fields of various sizes and shapes. Up to now it usually has been stated that 40 per cent should be added to the "air values" to arrive at a value of skin doses measured on the actual patient as expressed in roentgens.

The Desjardins anatomic charts,[2] which are widely used in roentgen therapeutic practice, have been used to obtain the following figures applicable to the problem of the roentgen treatment of inoperable carcinoma of the breast:

From the skin through the pectoralis major muscle, 4 cm.
From the skin to the pleura, 4.3 cm.
From the pleura to the center of the lung, 8.4 cm.
From the skin to the center of the lung, 12.5 cm.
From the skin over the sternum to the heart, 3 cm.
Diameter of lung, anteroposterior, 16.5 cm.
Thickness of breast, 4 cm.

[2] Section No. 3 (female) fourth intercostal space (midclavicular line).

TABLE I.—DEPTH DOSE WITH DIFFERENT TECHNICS

	Technic				
	A	B	C	D	E
	Set-up				
Kilovolts	135	135	200	200	200
Milliamperes	5	5	5	5	5
T.S.D., cm.	40	40	50	50	50
Filter, mm.	6 Al	6 Al	0.75 Cu + 1 Al	0.75 Cu + 1 Al	0.75 Cu + 1 Al
Field, cm.	10 by 10	15 by 15	10 by 10	15 by 15	20 by 20
Depth, cm.	Dose, per cent				
1	92	95	95	97	97
2	84	88	90	92	93
3	72	80	84	86	90
4	60	69	75	80	83
5	48	59	66	68	76
6	43	50	58	62	69
7	38	42	50	55	60
8	32	36	45	50	53
9	26	30	38	45	47
10	23	25	33	39	42
15	10				
16		10			
18			10		
21				10	
23					10

Anteroposterior diameter of the right side of the thorax, 21 cm.

From a study of breasts removed by radical operation, and some by "palliative operation," it was found that the average thickness of the specimen (including breast and pectoral muscles) was 4.5 to 5.5 centimeters. Naturally, the measurements varied with the thickness of the muscles excised with the breast, and with the amount of tumor in the breast, but surprisingly, the great majority of breasts which had been operated on were of the size given, within close limits. Rarely was a breast as thin as 3 or as thick as 8 centimeters. For all practical purposes of clinical dosage, it may be safely assumed that the average thickness of the inoperable breast also is 5 centimeters. Tumors of the breast 10 to 15 cm. in diameter, such as have been reported by others, have not been encountered. The measurements of the tumors in this series varied only slightly from the measurements of operative tumors.

With a hemispheric, superificial, solid body to treat, in which is embedded a carcinoma the radiosensitivity and pathologic and geometric relationships of which are peculiar, it hardly seemed logical to apply the usual technics of treatment worked out for either carcinoma of the uterine cervix or of metastatic nodes secondary to intra-oral carcinoma. However, in planning the technic it is obvious that roentgen rays generated at moderate or high voltage may be applied (Table I).

These values were obtained by making measurements of intensities of roentgen rays, with a thimble type ionization chamber placed in a block of wax of high melting point which in my experience has been easier to use than either the well-known water box or aluminum ladders, or even the common white wax of low melting point. With the apparatus these values have been uniform and have shown close agreement with the dose curves published by others. However, it is fair to assume a variable in their values, of ±3 per cent, this value being well within the clinical error of estimation of dosage. I have not had an opportunity to compare these figures with those obtained from a valve rectifier operating an autoprotecting type of tube.

By utilizing the well-known principles of cross-fire, the dose effective in a tumor may be increased. That the usual practice of a two-field cross-fire leaves much

TABLE II.—DEPTH DOSE WITH MULTIPLE FIELDS[3]

Depth (cm.)	Technic	Fields									
		1		2 opposite		3, 120°		4, 90°		6, 60°	
		Tumor	Lung	Tumor	Lung	Tumor	Lung	Tumor	Lung	Tumor	Lung
		Dose, per cent									
2	135 K.V.	83	35	83	100	249	105	332	140	498	210
4	4 mm. Al	60		60		180		240		360	
6		40		45		135		180		270	
8	E = 18 min.	34		34		102		136		204	
10		25		25		75		100		150	
2	135 K.V.	90	40	90	40–100	270	120	360	160	540	240
4	6 mm. Al	73		73		219		292		438	
6		55		55		165		220		330	
8	E =	38		38		108		144		228	
10	28 min.	30		30		90		120		180	
2	200 K.V.	95	50	95		285	150	380	200	570	300
4	$^3/_4$ Cu +	80		80		240		320		480	
6	1 Al	64		64		192		256		384	
8	E =	50		50		150		200		300	
10	70 min.	37		37	50–100	111		148		222	

to be desired has recently been emphasized by Desjardins, who pointed out that the use of multiple beams converging on a tumor from one surface may in many cases produce clinical response in cases in which the usual methods of cross-fire through two opposite fields have failed. But in treating carcinoma of the breast, the fact must not be lost sight of that radiation absorbed in the lung not only has nothing to do with the reaction of the tumor in the breast, but may actually be dangerous. Parenthetically, it might be mentioned that decrease of surface radiation intensity in the treatment of carcinoma of the breast, and abandonment of high voltage, have been accompanied by total disappearance of pleuropulmonitis. Even though it has been shown that the lung tolerates doses of roentgen rays which are safe for the skin, it is nevertheless a fact that cross-fire of a superficial tumor, such as a carcinoma of the breast, by overlapping of the beams in the depths of the lung may produce a dose beyond the limit of tolerance of the lung, even though the doses on the surfaces were well within safe limits (Table II).

In using these figures (Tables I and II) for applying a dose of roentgen rays to an inoperable carcinoma of the breast, two facts should be kept constantly in mind: the distance from the skin to the bottom of the inoperable tumor is usually less than 5.5 cm., and high voltage delivers a higher dose to the lung than is delivered by moderate voltage.

A glance at Table I will show that with Technic A, at a depth of 5 cm., the dose is 48 per cent, which means that 52 per cent of the incident radiation has been absorbed or scattered in the breast, or 52 per cent of 560 r, which equals 291 r. In Technic E, a high voltage technic, at a depth of 5 cm. the dose is 76 per cent, which means that 24 per cent has been absorbed or scattered; that is, 24 per cent of the incident 560 r, or 134 r. It seems self-evident, therefore, that in treating carcinoma of the breast moderate voltage is preferable, but if, on the other hand, the problem is to administer a dose to the lung, the cor-

[3] The following matters in this table require explanation: (1) E = erythema dose; (2) values were obtained by a different set-up for measurement than that used in Table I, yet agreement is close enough for clinical purposes; (3) T.S.D., used here, indicates distance from target to wall of thorax, not target to surface of the breast; (4) doses for the lung are measured 4 cm. below the pleura, and 8.5 cm. below the skin; (5) two fields at 90° equals the value of one field × 2; (6) in an anteroposterior cross-fire there is no appreciable increase in the dose that reaches the tumor from the posterior field, for the dose at 21 cm. in all types of radiation considered is 10 per cent (or less); (7) with technics employing 200 kilovolts it takes about 280 minutes for an erythema dose on four fields; (8) with 135 kilovolts, and 6 mm. aluminum filter, it takes about 112 minutes for an erythema dose on four fields; (9) the curves of dose show that 200 kilovolts produce an increase of about 40 per cent in depth effect with about twice as much time. According to a check-up by Failla, the values for multiple fields are slightly lower than those given here, because the angle of incidence is oblique and not vertical.

rect technic calls for the use of high voltage.

The number of fields through which the radiation is to be applied depends, primarily, on the size of the tumor. It is, therefore, impossible to do more than schematize the technics of treatment (Fig. 1). It might be mentioned that tiny inoperable tumors in the breast (up to 1 cm. sphere) are less effectively treated by this method than bulky tumors, because of the difficulty of cross-firing the smaller tumor. A moderately large tumor (2.5 cm. sphere) may well be treated by three converging beams; large tumors (3 to 5 cm. sphere), by four to six beams. The angles of incidence, the time of exposure, the use of 4 or 6 cm. aluminum filter, and so forth, must be individualized to fit the given case.

Because of the hopelessness of the condition to be treated, any crowding of the sessions of treatment is to be carefully avoided. Usually two fields are treated each day, so that the irradiation of the involved breast and of its regions of lymphatic drainage requires four to six days. It is extremely rare that such distribution of doses produces reactions severe enough to necessitate interruption of treatment. Since each field of treatment is outlined on the skin in indelible ink, and has its margins protected by several thicknesses of lead rubber and is treated with a suberythema dose, any marginal overlapping of fields of irradiation to the point of injury to the skin has not been observed.

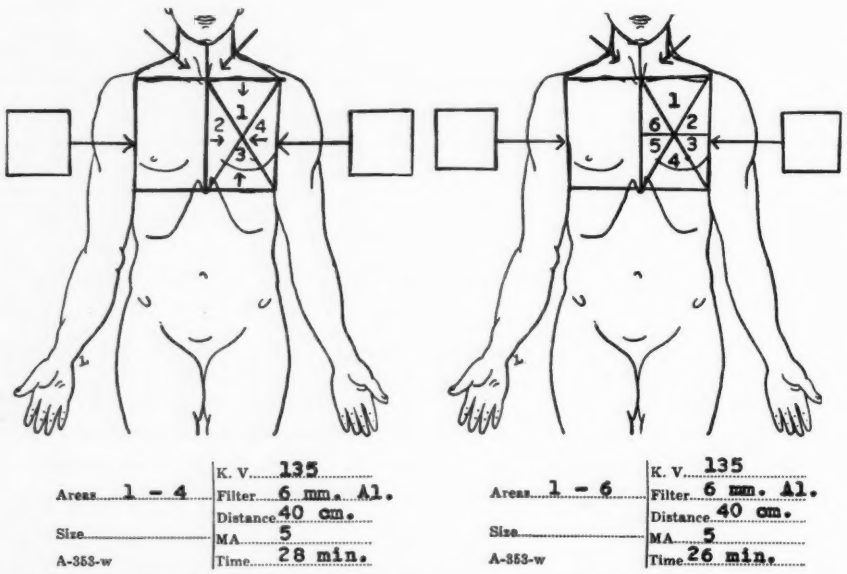

Fig. 1. The distribution of the fields of treatment. It may be noted that each area receives a suberythema dose of roentgen rays; the greater the number of portals the greater is the reduction of the dose to each.

Following the first course of treatment some improvement invariably results, so that unless there is some contra-indication, repetition of treatment is advised at intervals of three or four weeks until the tumor is clinically quiescent. Usually three courses (rarely five) are needed to produce this result.

From a clinical point of view this technic of converging beams, using roentgen rays generated at 135 kilovolts, has been found to be very effective in producing regression of the primary lesion. As was mentioned earlier in this paper, cure is out of the question in this group of cases. Since the natural duration of the car-

cinomas without treatment was so variable in this group, the effect of the treatment on duration of the patient's life was problematical. In the whole group, no effect, or a poor result, was obtained in two of the 41 cases, a questionable result in two others. In all of these cases not more than two courses of treatment were given, an amount which usually is regarded as insufficient. The condition of 37 patients was definitely improved. This improvement was manifested by clearing of the ulcer in ten of sixteen cases, by disappearance of cutaneous metastasis in four, and by cessation of hemorrhage and discharge in fourteen cases, benefits which were greatly appreciated by the patients and their relatives. This improvement has lasted in some cases for two years or longer, but, due to the systemic ravages of the disease, no patient is living, clinically well, beyond the accepted interval of five years. Since the improvement was achieved by a treatment well tolerated by the patient, it seems justifiable to continue its use in similar cases. However, since radiotherapy under the most favorable conditions has not as yet achieved results comparable with operation in large groups of cases, adoption of multiple converging beams for treating operable cases hardly seems indicated at present. That it is superior to high voltage technics seems to be demonstrated by this report.

CONCLUSIONS

1. In the method described, in which multiple converging beams are used, a higher dose of roentgen rays can be delivered to inoperable carcinoma of the breast than by any other method of external radiation.
2. Undesirable effects in the lung are minimized by this technic.
3. The treatment is well tolerated by the patient.
4. The results obtained in treating 41 patients with inoperable carcinoma of the breast justify continuation of the use of the method.

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THE INFLUENCE OF THE ANTIQUITY OF THE CELL UPON CELL RESISTANCE TO RADIUM AND X-RAYS[1]

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THE object of this paper is to present certain evidence which indicates that those cells which have existed on the earth in an unchanged condition for a long period of time, have probably acquired a resistance to short wave radiation by reason of continued exposure to the radiation in the crust of the earth, and from cosmic rays, and that a careful consideration of this fact may be of value in advancing the efficiency of radiation therapy of malignancy.

The resistance of both animal and plant cells to the rays of radium and x-rays has been of great interest to radiotherapists, as well as other scientists. Of the many biologic problems in radiation therapy, that of cell resistance is the most interesting and of greatest practical importance to the physician.

The idea that cells may have developed a resistance to short wave radiation in Nature is not new, but the application of the idea as made in this paper is original.

There is a vast amount of literature bearing upon the question of resistance of various organisms to radium and x-rays, the great part of which is of but little value because of lack of proper measuring and recording of dosage, and the fact that many of the early observers based their opinions on the immediate effect produced. Therefore, only a few of the more recent well-controlled experiments are referred to in this paper.

We are well acquainted with many factors, such as the type and age of the cell, rapidity of division, and chemical composition, which affect the resistance of cells to radiation, while for many years we have been interested in the question of whether or not a cell may develop a resistance to radiation as a result of the application of radiation. It seems that, since a plant or animal will become acclimated or accustomed to a change in physical surroundings, if the change be brought about gradually enough, a like tolerance may be produced by short wave radiation, provided the radiation be applied in proper quantity, and over a sufficient length of time.

Radiologists frequently observe clinical evidence of the development of resistance to radiation during the application of radium and x-ray to malignant tumors; as when tumors at first show a marked reduction following a dose of radiation, and at a later date fail to reduce, or may even show a rapid growth, following the same or a larger dose. Of course, this is not positive evidence that direct stimulation of cell resistance occurs as a result of the direct action of radiation, but in the light of experimental evidence at hand, it is strongly suggestive that such resistance is developed.

There is a vast amount of experimental evidence to show that cells develop a resistance to radium and x-rays. I was able to produce a resistance to x-rays in wheat plants by giving 3,000 roentgens to dry wheat seeds five days before planting. Plants from such seeds showed 30 per cent greater resistance to the same amounts of x-rays than controls, while 200 roentgens was found to be a stimulating dose to sprouting wheat seeds, the plants showing a growth 15 per cent more rapid a week after raying. Charles A. Shull has reported similar stimulation of wheat, corn, oats, and sunflowers (1). He has more recently shown that resistance to x-rays can be created in plants by small doses of x-rays (2).

One of the most convincing arguments in favor of the idea that cells remaining for a long period of time on earth, in an unchanged state, have developed resistance to radiation is the fact that, as a class,

[1] Read before the American Congress of Radiology, Chicago, Sept. 25–30, 1933.

unicellular organisms are much more resistant to radium and x-rays than are the cells of multicellular organisms.

We know that many of the deeper rocks of the earth's crust are made up largely of unicellular organisms which existed many hundreds of millions of years before multicellular life appeared on the earth. Dr. White, of the U. S. Geologic Survey, has found *Alga*, the first living cell known to exist on earth, in the deepest structures of the earth. I have found *Alga spirogyro* to be highly resistant to x-rays. Some specimens have been growing in my laboratory window for the past month, after having received 75,000 roentgens; some are living, but show retardation of growth, two months after receiving 150,000 roentgens.

Further evidence to support this theory is the well-known fact that plant cells, as a class, show a much greater resistance to radium and x-rays than animal cells do, and we have good evidence that plants are more ancient than animals. Biologists advance the idea that plants must have existed before animals to furnish food for the animals.

We assume that a cell which has remained longest on the earth in an unchanged state would retain its maximum acquired resistance to radiation, and that, if such a cell should undergo a change, it might thereby lose a part or all of its acquired resistance to short wave or other forms of radiation.

Another interesting question, as suggested by Haldane (3) in regard to cells developing a resistance from radiation found in Nature, is whether or not the beta rays from potassium in plant cells may produce such resistance. P. H. Haskins has reported a vast difference in the resistance of plants and seeds to x-rays. For instance, he finds that the bulbs of Regal lilies are highly sensitive to x-rays and are killed by 1,200 roentgens, while bulbs of narcissi will withstand 40,000 roentgens. A chemical analysis reveals that these two kinds of bulbs contain the same amount of potassium (0.27 per cent), so that this difference in resistance cannot be attributed to difference in amount of beta rays of potassium contained in the bulbs.

Another plant which is resistant in a marked degree to radiation is the family of ferns, a plant form which paleontologists estimate to be about two hundred million years of age. Dr. Lewis Knudson, of Cornell, has found that from 2,500 to 5,000 roentgens is a stimulating dose to ferns, and from 7,000 to 30,000 roentgens is required to stop their growth. In my own work I have found ferns to be about the most resistant of plants to x-rays. A fern which received 90,000 roentgens remained perfectly green for six months without exhibiting any signs of growth or reproduction. This fern may be like the x-radiated worm of which Curtis (4) commented that he questioned it having the ability to die. We usually find that death does not so frequently occur in x-radiated algæ and scorpions as in the controls.

The work of H. K. Svenson (5) shows *Saprolegnia*, of the family of *Fungi*, to be highly resistant to x-rays. Molds belong to the same age as algæ. Protozoa are found to be markedly resistant to x-rays.

The cells of man are about the most sensitive to radiation, and we have reason to believe that man is about the youngest animal on the earth.

It seems that the source of the radiation which has produced cell resistance is an important question, especially since we have some clinical and experimental evidence to suggest that there is a difference in the biologic effect of different wave lengths. In this connection at least three types of radiation must be considered: First, the beta rays, as from potassium, present in all cells, and uranium, which has a wide distribution. Then come the gamma rays of radium—present at this period in small quantities throughout the crust of the earth and probably present in much larger quantities a few million years in the past. Third, we have good reason

to believe that the very short wave cosmic ray has probably bombarded the earth from all directions throughout the entire existence of the latter, and with probably a rather constant intensity.

We have but slight direct proof of the fact that these various sources of radiation are responsible for the development of resistance of cells to radiation, but we have a vast amount of circumstantial evidence to indicate that such resistance is the result of bombardment by the very short gamma rays and the cosmic rays. Then we must consider the fact that, if there is a difference in the biologic effect of rays of different wave lengths, a resistance created by a very short wave length, as the shorter gamma ray and the cosmic ray, does not necessarily mean a resistance to the longer wave lengths. Therefore, the acquired resistance of normal cells may be an important factor in explaining the apparent selective action of short wave gamma and x-rays on cancer cells—the cancer cells, having undergone a change, may have lost their acquired resistance to such rays.

This subject is presented with the hope that further investigation of it may aid in solving the great problem, namely, Why are superior clinical results obtained in our modern method of the treatment of cancer by short wave x-rays and gamma rays of radium? Also, it may furnish an answer to the problem of the employment of x-rays produced by a million or even many millions of volts.

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BLASTOMYCOSIS OF THE SKELETAL SYSTEM

A BRIEF REVIEW OF THE LITERATURE, WITH A REPORT OF THREE ADDITIONAL CASES

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ACCORDING to Castellani (5), "The term blastomycosis covers all conditions due to yeast-like fungi, but from a practical point of view it is of advantage, as is usually done in this country, to limit its meaning to denote solely or principally a clinical entity or, more correctly, a group of closely allied entities characterized by the presence of granulomatous, verrucoid lesions in which fungi of the type *Blastomycoides* are found." Furthermore, he continues, "The term blastomycosis covers a group of closely allied pathological conditions due to fungi of the genera *Saccharomyces*, *Cryptococcus*, *Coccidioides*, *Odium*, and *Monsilia*, generally characterized by the presence of warty patches and minute epidermal abscesses."

Stoddard and Cutler (24), in 1916 (writing only two years before Castellani) predicted, "The name blastomycosis will eventually be applied to a group of diseases produced by various organisms." They agree with McNeal and Taylor who concluded that "blastomycosis and coccidioidal granuloma are distinct clinically, pathologically, and biologically."

In this report Stoddard and Cutler's (24) views have been followed.

Historical.—These same authors are cited as follows: "Weinike, in 1890, described in Buenos Aires two cases of papillomatous eruption in which he found peculiar bodies which were at first considered to be protozoa, hence the disease was called 'protozoic dermatitis.' Later Gilchrist and Ophüls showed them to be vegetal parasites. Gilchrist, in 1894, described yeast-like organisms in sections taken from a scrofuloderma-like eruption. In the same year, independently, Busse and Buschke published a case of a pyemia-like condition due to a *Cryptococcus*."

From the Department of Roentgenology, State University of Iowa. Received for publication Dec. 28, 1933.

It is interesting to note that Busse's case was one in which the tibia was involved. The area was removed surgically. Lesions of the face, neck, right ulna, and sixth left rib followed. The patient died five months after operation, autopsy revealing numerous foci, from all of which the blastomycetes could be cultivated. And yet Buschke did not differentiate coccidioidal granuloma and blastomycosis.

Incidence.—Since 1919 only two other cases of blastomycosis (both of the skin), proven by finding the organism, are on record at University Hospital, University of Iowa. In 1902, F. H. Montgomery (19) summarized the cutaneous features and reported 13 cases of generalized blastomycosis, yet in only two of these cases were the bones involved.

Bassoe (2), in 1906, had a case of involvement of the scapula.

In 1907, Herrick (10) reported one case, and in 1908 Ryerson (22) reported two cases.

In 1908, Ormsby and Montgomery (18) reported 22 additional cases of systemic blastomycosis, but only seven of these had involvement of the skeletal system.

Washburn (28), in 1911, and Stober (23), in 1914, each had one case.

Wade and Bel (26), in 1916, had collected a total of 27 cases of systemic blastomycosis and in only 16 of these were the bones involved. They included the report of Ormsby and Montgomery.

Howe (11) in 1921, Garr (8) in 1925, Medlar (15) in 1927, Toepel (25) in 1929, Jones (12) in 1930, and H. Montgomery (20) in 1930 each report one additional case.

Thus, including the three cases which are being reported at this time, only 32 cases of blastomycosis of the skeletal system are on record.

Morphology.—To quote Castellani (4) further: "Morphologically, in the lesions,

two principal types of yeast-like fungi may be distinguished: (*a*) the blastomycetoid (blastomycetic) type; (*b*) the crystococcoid (sacchomycetic) type. The characteristics of the blastomycetoid type are the following: Cells large, double contour, with very well marked granules or spherules in the protoplasm, very evident and of comparatively large dimensions. The characteristics of the crystococcoid type are the following: Cells generally smaller, double contour absent, or much less marked, protoplasmatic granules not so evident and usually much fewer."

Wade and Bel (26) state: "The typical so-called blastomyces in the tissue lesion do not produce mycelia and do not form ascospores, but appear and persist in the form of more or less sclerotic yeast cell-like bodies which multiply by budding."

Ottis and Evans (21), Washburn (28), Jones (12), and Medlar (15) also stress the fact that the organisms are spherical or oval, double-contoured, with very refractive cell capsule, and increase by budding.

Pathology.—The pathology in blastomycosis differs little from that of tuberculosis (9, 12, 17). Occasionally it does differ from tuberculosis in that there may be less central necrosis when seen microscopically.

Mode of Extension.—Montgomery and Ormsby (18) conclude that, "The mode of extension is the same as in other pyemias, through the blood instead of by way of the lymphatics, as is evident from the wide and often rapid dissemination of deep-seated lesions, with little or no involvement of the lymph glands, and from the fact that blastomycetes have been demonstrated in the blood." This point is well taken, as Malroy and Ricketts (13) have demonstrated a complement deviation test in blastomycosis, using old cultures of blastomycetes as antigen. Also, Helstoen (7) found that "the undiluted serum of a dog which had received successive inoculations from a case of cutaneous oidiomycosis, caused gradual clumping of the yeast in bouillon cultures."

Stober (23) and Ryerson (12) both agree that, as far as the long bones are concerned, "the infection has a tendency to lodge in the epiphyses and in some instances the shape of the infected area strongly resembles [one of] those produced by infarct. Extension by rupture of the epiphyseal abscesses is responsible for the majority of the joint lesions."

Howe and Morse (11), also Stober (23), conclude that the portal of entry is probably by way of the respiratory tract, although in the case reported by Toepel, the portal of entry was a thorn prick on the left index finger. Also, in one of our cases no evidence of any pulmonary involvement has been found to date.

Whereas D'Amoy and Beven (6) feel that "the occurrence of visceral blastomycotic involvement is secondary to cutaneous lesions caused by the parasites, but this does not necessarily follow."

Clinical Classification.—Castellani (5) makes a clinical classification as follows: (1) Common cutaneous type, (2) the oropharyngeal, (3) the coccidioides, (4) gluteal blastomycosis. This classification is one of interest as it indicates the close relationship of blastomycosis and coccidiosis.

Diagnosis.—Diagnosis rests on finding the characteristic organism. The similarity to tuberculosis of the pathologic findings is well known. In regard to the lung W. S. Miller (17) says: "This study of the reticulum shows that its growth and transformation into collagenous tissue differ in no way in the tubercle of blastomycosis from that of the tubercle of tuberculosis." Also, "If the presence of the special organism be eliminated from the picture, the lesion is the same in both infections." Montgomery and Ormsby (18) also write: "Giant cells and other cells peculiar to the granuloma have been observed in several instances," while Ricketts (24) adds, "The nodules and giant cells of cutaneous oidiomycosis are indistinguishable from those of tuberculosis." Similar views are held by Medlar (15) and Stoddard and Cutler (24), who wrote:

"The striking similarity of the lesions, both gross and microscopic, in the two classes of infections is undoubtedly outstanding. . . . Still, such a similarity in lesions produced need not be surprising, when we consider that new methods of investigation seem to indicate biologic relationship between the fungi and those microorganismal forms classed as acid fast."

As regards the diagnosis of blastomycosis from that of coccidiosis, Stoddard and Cutler (24) show that: (1) true budding is not found in coccidioidal granuloma but is constant in blastomycosis; (2) coccidioidal granuloma sporulates in tissue while blastomycosis does not.

As to x-ray diagnosis, Potter, quoted by Stober (23), believes that, "A marked localizing destruction occurring within the spongy bone of a diaphysis, together with a mature and homogeneous periosteal proliferation with or without cloaca, is so constantly present in the ordinary lesions of blastomycosis that when seen in further skiagraphs, where the etiology has not been determined, a careful search for blastomycetes should be made."

Carter (3) believes that coccidioidal granuloma should be considered separately from blastomycosis, yet roentgenologically, he admits, they cannot be separated. Thus from a roentgenologic standpoint, tuberculosis, coccidioidal granuloma, and blastomycosis must be considered together and the final diagnosis made from finding the causative organism.

Prognosis.—F. H. Montgomery (19) in 1902, Herrick (10) in 1907, Marshall (14) in 1929, and Altschul (1) in 1930 each report a case of generalized blastomycosis with recovery. No other cures have been found. It is possible that Herrick's case did not have bone involvement as x-rays were not common at that time and the surgeon merely drained the gluteal abscesses without exploring the pelvic bones. This same criticism would apply to Montgomery's case, though the lesions were scattered and involved the left hand, left leg, left heel, right palm, left breast, and tenth and eleventh interspaces.

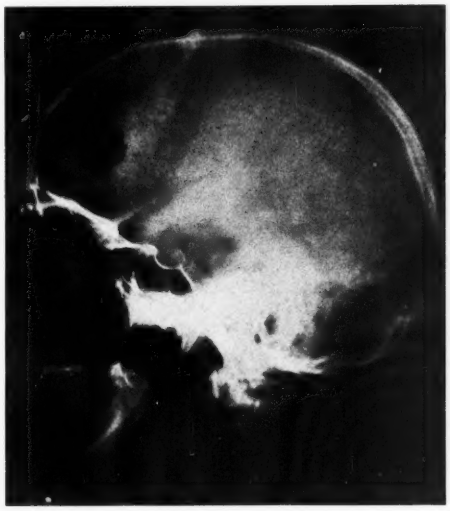

Fig. 1. Lateral skull, Case 1, from which a diagnosis of syphilis was made.

Thus the prognosis of blastomycosis of bones is bad, because it is usually but a manifestation of a systemic condition, although two of our cases are in good condition—ten months and five months, respectively, since diagnosis.

Treatment.—Iodides by mouth and intravenously are still the main means of therapy. Unfortunately, patients are sometimes moribund before a diagnosis is reached, as occurred in our first case. The other two cases have tolerated huge doses of iodides and have improved. Autogenous vaccine was first suggested by Christensen (7), and Hektoen and Stober (7) report that autogenous vaccine was of value in two cases; also since Helstoen (7) has demonstrated immune bodies in the blood stream, vaccines should be attempted. They have not been used in our cases. X-ray therapy in the skin lesions is of value and we feel that radiation therapy should be attempted in the bone lesions. Unfortunately we have not been allowed the opportunity as the two living cases have done so well on iodides, and the patient in whom the disease was fatal died a few days after our attempts to relieve his pain by x-ray. We gave him 200 r, with 0.25

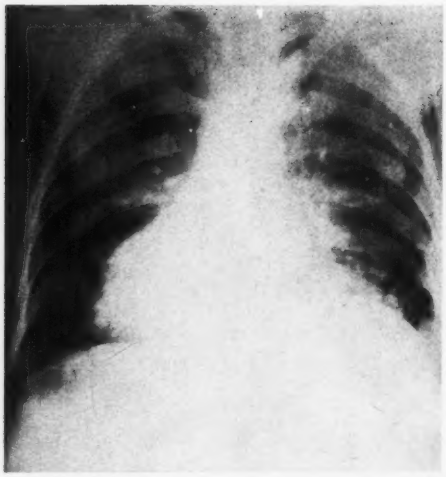

Fig. 2. Roentgenogram, Case 1, from which the possibility of a fungus was suggested as the cause of pathology.

Fig. 3. Lateral spine, Case 1, showing marked destruction of the body of the eleventh thoracic vertebra, most of the destruction having occurred within a period of three weeks, as seen by earlier films.

mm. Cu and 1 mm. Al, at 140 K.V., 5 ma., with a field of 400 sq. cm. at a distance of 50 cm. over the lower thoracic spine, a method which we have found to be of value in the relief of pain from malignancies of bone. No apparent relief was obtained.

Fig. 4. Right ulna, Case 1, showing involvement of the head. This film was taken two weeks later than the one shown in Figure 3, and indicates the rapidity with which the disease spread.

Case Reports.—Case 1,[1] A. H., white, male, aged 41 years, was admitted to the medical service of University Hospital Aug. 22, 1930. The onset of symptoms dated from April, 1930, and consisted of pain in the back and upper abdomen. A laparotomy elsewhere gave no relief although a pathologic appendix and adhesions were found. About May, 1930, a small hard lump appeared in the left frontal region, a lump which did not cause pain and grew slowly in size. Examination on entrance revealed a soft tumor mass in the left frontal region about 4 cm. in diameter. Just above the corner of the mouth was a small erythematous, darkly crusted lesion. A similar skin lesion was

[1] Previously reported by Dr. C. Cooper, Jour. Iowa Med. Soc., March, 1931, XXI, 119.

noted on the left forearm. While in the hospital a swelling of the lateral aspect of the right foot was drained and sterile pus obtained. On Sept. 11, 1930, a definite gibbus in the lower thoracic region was noted. Pus from the frontal abscess was negative for tubercle bacilli after guinea pig inoculation. The sputum was negative for fungi and tubercle bacilli; repeated Wassermann tests were negative (both blood and spinal fluid, although the spinal fluid contained 135 cells). Three days before death blastomycetes were isolated from the skin lesions of the face. Autopsy revealed blastomycosis of lungs, prostate, frontal bones, olecranon process of the right ulna, ninth and tenth dorsal vertebræ, and skin lesions of the face.

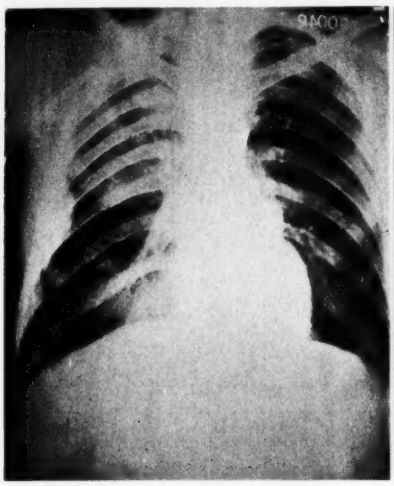

Fig. 5. Roentgenogram, Case 2, showing abscess of right lateral chest wall and fibrosis at the right base.

Fig. 6. Oblique view of upper right chest wall, Case 2, showing the origin of the abscess seen in Figure 5.

Case 2, J. C., white male, aged 42 years, was admitted to the hospital on Nov. 17, 1930, as a private patient of Dr. F. M. Smith, referred by Dr. Wolverton, of Cedar Rapids, Iowa. Family and past history revealed no essential facts. Patient has had a persistent cough for last few years, with yellow sputum. In February, 1930, he first noticed a skin lesion on the right knee, then one on the left shoulder, and one on the right cheek. He has had pain in the middle of the back since July, 1930, and came to the hospital because of general weakness. Examination revealed the percussion note to be definitely impaired in the right apex and in the inter-scapular area on the left side posteriorly. On the anterior chest to the right of the sternum was an area of swelling about the size of the palm of the hand. On the right cheek, right hand, and left shoulder were skin lesions characterized by a central area of healing. Blastomycetes were isolated from the skin lesions but not found in the sputum. Patient has greatly improved on large doses of iodides both by mouth and intravenously, and in July, 1931, was in good condition.

Case 3, L. J. L., white male, aged 47 years, was admitted to the hospital July 15, 1931, to the surgical service. Family and personal histories were irrelevant. In March, 1931, the patient injured his right wrist in cranking a car, and broke the skin of the palm, whereupon the wrist soon became sore and tender. About six weeks later the wrist began to drain and drainage continued until July 1, 1931. In May,

Fig. 7. Pelvis, Case 2, showing the punched-out areas of destruction, especially to be seen in the left pubic bone.

1931, the right tibia became painful without trauma, but did not drain pus until July. Blood Wassermann was negative. Several fragments of carpal bones were removed and the lesion of the tibia drained. Pus specimens from wrist and tibia were negative for tubercle bacilli by guinea pig inoculation, but grew blastomycetes on culture. Sputum was negative for fungi. Patient has improved symptomatically on iodides by mouth and copper sulphate locally.

Discussion.—Our first case was admitted as a case of syphilis and the first film, which showed the skull defect, tended to prove this. Chest films, however, were suggestive of a mycotic infection and the bone condition, as shown in the spine, was diagnosed as a fungus lesion of some type until the organism was found.

The second case was diagnosed correctly, as our first case was still fresh in our minds.

The possibility of blastomycosis was made clinically in the third case, but the portal of entry cannot be determined as the lungs have yet to show any pathology. The broken skin of the palm would indicate that as the portal of entry.

Fig. 8. Wrist, Case 3, showing destruction of end of ulna, with beginning involvement of the carpal bones.

SUMMARY

1. Only 32 cases of blastomycosis of the bones have been reported.

2. Blastomycosis of the bones is usually a manifestation of systemic blastomycosis, and so local therapy, such as excision, is not sufficient.

3. A complement deviation test might prove of value in diagnosis, and autogenous vaccine in therapy.

4. Tuberculosis, coccidioidal granuloma, and blastomycosis produce the same pathology.

5. We feel that the possibility of blastomycosis should be considered in all chronic

osteomyelitic lesions and the pus examined for blastomycetes.

I wish to thank Dr. F. M. Smith for permitting me to use his private records.

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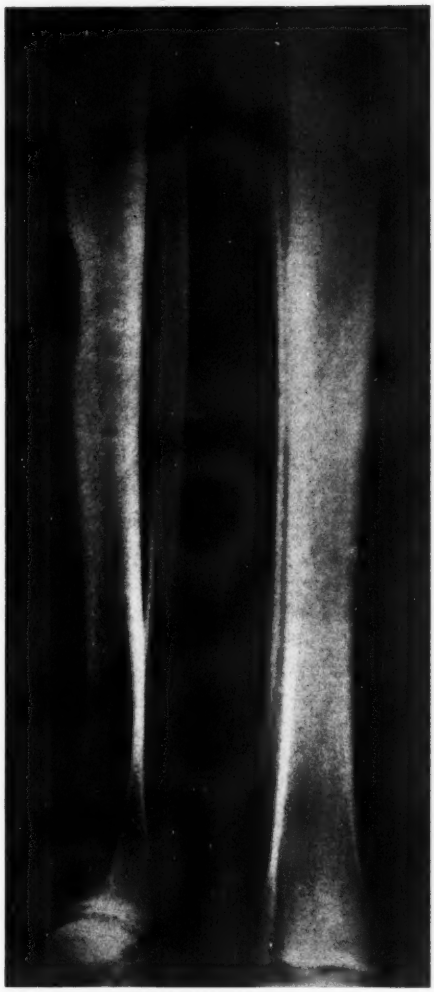

Fig. 9. Tibia, Case 3, showing the defect in the upper third. At the present time this defect is entirely healed.

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HEAT PRODUCTION IN DIATHERMY TREATMENTS[1]

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A MATTER of interest in the clinical use of diathermy is the total amount of heat in calories which is received by the patient during a treatment and the rate at which this heat energy is delivered. This is especially important in view of the recent efforts of the Council of Physical Therapy of the American Medical Association to standardize and improve diathermy machines. It is necessary to know the amount of heat energy required for a proper treatment before requirements can be made for the manufacture of suitable diathermy machines for clinical use.

It is the purpose of the following measurements to determine: (1) the total amount of heat in kilogram calories which a patient receives during a routine treatment, and (2) the rate at which heat energy is generated within the tissues. This latter value is most conveniently measured in watts and represents the high frequency power output of the diathermy machine. The physical relation is

1 watt = 4.19 gram calories per second.

Theory.—The measurements were made by means of a high frequency thermocouple voltmeter connected in parallel with the patient and a high frequency ammeter in series with the patient. From alternating current theory it is known that the heat production in calories per second is given by the relation $0.24\ VI \cos \theta$, wherein V is the reading of the voltmeter and I is the current in amperes. From earlier work (1) on plant tissues and more recently (2) on diathermy patients, it has been shown that at the high frequency of the diathermy current the "power factor" $\cos \theta$ is equal to unity, although at lower frequencies it may be considerably less than unity. Hence, since $\cos \theta = 1$, the high frequency power is $0.24\ VI$ calorie per second.

Experimental.—The patients used were those undergoing diathermy treatment at the University Hospital of the University of Minnesota with the diathermy doses of current intensity and duration time of treatment as prescribed by the Staff of the Hospital. In one group of experiments the total heat production and power output were measured by a thermocouple voltmeter and ammeter. For a voltmeter a specially constructed model 492 Weston thermocouple voltmeter was used. The ammeter used was the thermocouple ammeter in the diathermy machine.

Preliminary tests were made on two voltmeters and two ammeters using the four possible combinations of the two instruments. The heat production was measured calorimetrically (3) by using electrolytic solutions having resistances of the same order of magnitude as a patient. The following is the result of a single test:

Rate of heat production measured calorimetrically	= 29.7 watts
With voltmeter (1) and ammeter (1) V_1I_1	= 27.4
With voltmeter (2) and ammeter (1) V_2I_1	= 30.2
With voltmeter (1) and ammeter (2) V_1I_2	= 25.6
With voltmeter (2) and ammeter (2) V_2I_2	= 28.3

Thirty-six similar tests were made, varying the solution resistance, spark gap interval, the diathermy machine, and the coupling inductance, and the correction factor for a particular machine, voltmeter, and ammeter was determined. Thus with a Victor diathermy machine which was used, with the "voltage" and "frequency" connection fixed and the same ammeter and voltmeter throughout, it was found that by multiplying the observed voltage x current by the correction factor the true heat production was computed. This correction factor varied with the energy production, but

[1] Aided by a grant from the American Medical Association.

was independent of the spark gap interval and the resistance of the solution. The correction factor for different power values is given in Figure 1. Thus, in order to obtain the true power, the product I × V must be multiplied by the correction factor corresponding to the value of I × V.

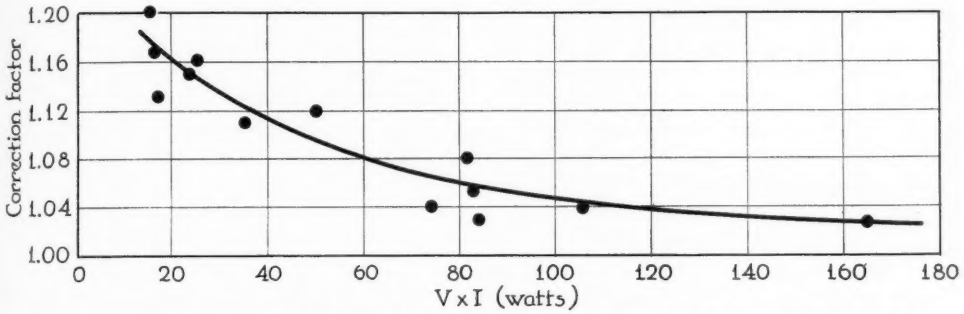

Fig. 1. Correction factor for Victor ammeter and Weston 125-volt voltmeter, Victor diathermy machine.

The results of a series of measurements are given in Table I.

The two types of electrodes used are the pliable tin electrode, designated as *M* in the table, and the saline pad, designated as *P*. Other values of the high frequency power output can be obtained from an earlier paper (3) wherein high frequency resistance values of patients and the diathermy current are given. The power output is I^2R. If the I^2R values are calculated, it will be seen that they are of the same order of magnitude as those in Table I. In this earlier work no correction was made for the ammeter, but the reading of this instrument is approximately correct as other data in the same table indicate.

Results.—In local diathermy, *i.e.*, treatments of joints, extremities, and regions of the trunk, as distinguished from general diathermy wherein the whole body is heated by a massive dose, it is found that the high frequency power received by the patient varies from 10 to 218 watts, while the majority of treatments are less than 100 watts. During treatments lasting 30 minutes the heat energy from the electrical current alone, which is produced in the tissues of the patient, varies from 15 to 60 kilogram calories of heat.

Discussion of Results.—Diathermy machines which are to be used for local diathermy treatments must be capable of producing up to 250 watts of high frequency electrical energy. The frequency of the current must also be sufficiently high to prevent neuromuscular response, and with this high energy output there must be no unbalance of the circuit resulting in faradic stimulation due to low frequency pulses.

These results enable a standard to be

TABLE I.—ENERGY AND POWER PRODUCTION DURING DIATHERMY TREATMENTS

Type	Area (1)	Area (2)	Region	Current	Voltage	Time	Power (watts)	Total Heat (calories)
M	9 x 16	9 x 16	Shoulder	1.0	51	30	56.1	24.2
M	15 x 11	18 x 16	Hip	0.97	66	30	69.2	29.8
M	24 x 20 (post.)	24 x 17 (ant.)	Thoracic	2.1	102	30	218.0	94.5
M	15 x 11	18 x 16	Hip	1.0	53	30	57.8	25.4
P	9 x 13	42 cm. Cuff	Thigh	1.5	93	25	145.0	52.4
M	9 x 13	9 x 13	Hip	1.0	56	30	61.0	26.4
P	8 x 10	8 x 10	Knee	0.80	43	30	39.2	16.7
M	9 x 16	9 x 16	Shoulder	0.90	52	25	51.5	56.7

set for diathermy machines. They must be so constructed that they are capable of generating enough energy to produce sufficient local hyperthermia. The values which are given are those which have been found to be satisfactory for routine clinical treatments by the Staff of the University Hospital of the University of Minnesota.

Another important aspect of this problem is the possibility of studying the physiologic response of the patient to measured dosages of heat. By means of the system described, it is possible to apply any predetermined number of calories to any part of the body over any desired interval of time. The physiologic response, *i.e.*, temperature rise, increased blood flow, cardiac response, etc., may vary in certain normal and pathologic conditions and the difference in response may be of importance in diagnosis. This is a matter for future research.

These experiments were carried out with the co-operation and assistance of Dr. Stenström and his Staff of the Department of Physiotherapy of the University Hospital. I would like to take this occasion to express my appreciation of their interest and co-operation.

I also wish to acknowledge a grant from the American Medical Association for the purchase of apparatus.

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LEAD POISONING IN INFANTS AND CHILDREN

ROENTGENOLOGICAL FINDINGS[1]

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LEAD poisoning in infants and children is, unfortunately, of relatively common occurrence. In the past nine years, 95 cases have been observed in the Infants' and Children's Hospitals of Boston, and in the past twelve months (to September, 1933) 19 patients were admitted to the hospital with symptoms of intoxication directly attributable to this cause.

It is not within the scope of this paper to discuss in detail the etiology and clinical features of the disease. An extensive résumé of lead poisoning has been published by Aub and his co-workers and recently a review of the manifestations of the disease in children has appeared (1, 8). However, a brief description of the sources of lead and symptomatology, together with an evaluation of certain special signs and tests, is desirable in determining the proper place of the roentgenologic findings as aids in the diagnosis.

SOURCES OF LEAD

Lead poisoning in children is due usually to the ingestion of lead paint, chewed by the child from the toys, crib, or woodwork of the house. Small amounts of lead in drinking water may lead to intoxication. We have seen one case of lead poisoning following the eating of fruit which had been sprayed with lead arsenate. In infants, prolonged use by the mother of lead nipple shields (14) or the application to the breasts of lead acetate ointment has resulted in intoxication. In Japan, poisoning of infants has occurred frequently from the use by the mother of face powder containing lead (3, 4, 5). Recently an extensive series of cases has been reported of poisoning following the inhalation of fumes in homes where casings of storage batteries were used as fuel (15).

The development of symptoms following the ingestion or inhalation of lead appears to depend upon the age of the child, the amount of lead absorbed, and the period of time over which it is taken in, as well as individual variation in tolerance. The poisoning by lead of all the young patients we have seen has been a gradual process. Whether from paint, water pipes, or nipple shields, the ingestion of small amounts of the metal has gone on for weeks or months before the patient was brought for medical attention. Thus we usually see the culmination in acute symptoms of what is actually a chronic poisoning.

When lead is absorbed it is probably carried to all parts of the body, the major portion soon being deposited in the bones in inert form (1). However, lead as well as other minerals is always in a state of flux between deposition and resorption; small amounts are constantly being eliminated. Under certain circumstances the lead deposited in the bones may be mobilized again to enter the circulation and cause symptoms of disease. A patient whose bones contain deposits of lead may be spoken of, therefore, as having latent lead poisoning. Acute, febrile illnesses or acidosis appear to be the important factors influencing the mobilization of lead, changing a latent into an active type of poisoning.

SYMPTOMS

The complaints for which children with severe lead poisoning are brought to the

[1] Read before the American Congress of Radiology, Chicago, Sept. 25–30, 1933.

Fig. 1. R. M., female, aged 2½ years, admitted Oct. 3, 1932, on account of irritability, ataxia, tremors, drowsiness, and vomiting—becoming progressively worse for three months. Had been chewing paint for at least four months, probably longer. Roentgenograms on admission showed heavy lead lines in the long bones and separation of the cranial sutures shortly after admission. Blood contained numerous stippled R.B.C. and spinal fluid increased cells and globulin. Intracranial pressure was greatly increased. Encephalogram made after the acute symptoms had subsided shows enlarged ventricles (brain atrophy). Although the sutures are still separated there is no longer increased pressure. Child is defective mentally and almost completely blind.

hospital are vomiting and convulsions. On questioning the parent, one usually finds that for a considerable period the child has been nervous, fretful, constipated, and perhaps somewhat anemic. Occasionally the child has been considered a behavior problem.

Disturbance of the central nervous system is indicated by the development of projectile vomiting, ataxia, muscular twitchings, and slight stiffness of the neck, followed by stupor, lethargy, and generalized convulsions.

After the development of the encephalitic process which is the usual form of the disease in children, the blood pressure is usually elevated, the pulse and respiratory rates may become slower than normal, examination of the eye grounds may show choking of the optic discs, and occasionally separation of the cranial sutures is observed by roentgenogram (Fig. 1).

Even though the patient survives acute lead encephalitis he may sustain permanent cerebral injury inasmuch as the central nervous system seems to be especially susceptible to damage from deposition of lead. Of the 19 cases with symptoms seen during the past year, three died, while at least three of the 16 surviving have symptoms of residual damage such as cerebral palsy, epileptiform seizures, partial blindness, and mental deficiency.

In the less severe types of intoxication, instead of symptoms of disturbance of the central nervous system, patients may have vague gastro-intestinal complaints, anorexia, constipation, and abdominal cramps. If associated with vomiting at this stage, the symptoms often suggest some intra-abdominal surgical condition.

Lead neuritis, encountered in adults with plumbism, is not common in childhood, but it does occur; the resulting weakness of the extremities may lead to confusion of the condition with poliomyelitis. One small girl, subsequently proved to be suffering from lead poisoning, complained of pain in the legs and difficulty in walking, and was referred to her family physician as a case of rheumatic fever. Recovery was complete when she was prevented from eating any more paint.

Thus far no satisfactory therapy has been developed for patients in the severe encephalitic stage of lead poisoning. Although the outlook must be pessimistic in patients suffering from lead encephalitis, recovery seems to be quite rapid and complete in the milder types of the disease in which symptoms are recognized early and the ingestion of lead promptly stopped. The early and accurate diagnosis of the condition is therefore of paramount importance.

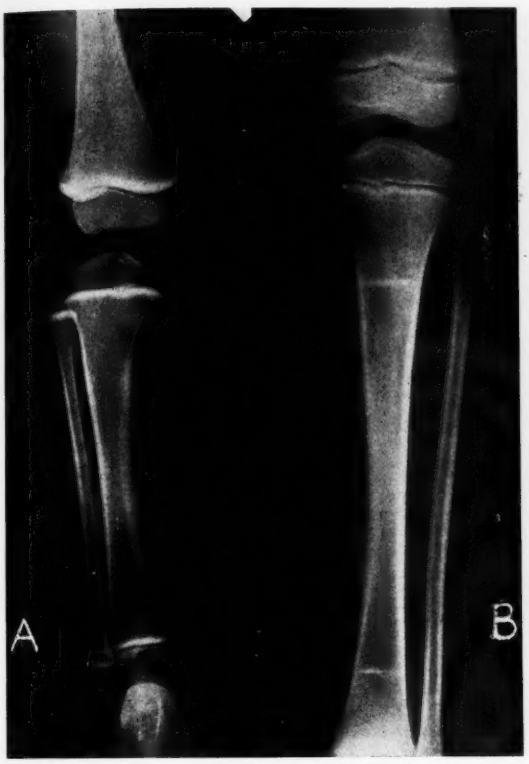

Fig. 2. M. O., aged 2 years. (*A*) Lead bands in the growing ends of the long bones. Film made May 27, 1930, at the time of acute lead poisoning. (*B*) The same patient almost three years later (Feb. 15, 1933). Child has entirely recovered but scars are still present in the shaft of the tibia and the epiphyses of the tibia and femur at the exact site of the previous lead bands. It is probable that all the lead has been eliminated, but the persisting scars suggest that the lead has produced changes in the bone structure itself, *i.e.*, an actual osteitis or osteopathy.

Fig. 3. L. P., male, aged 2 years 9 months, admitted on account of irritability, difficulty in walking, failure to talk, and incontinence. Mother said he had always chewed paint from the furniture and toys. Note a broad zone of increased density at the ends of the long bones, indicating prolonged deposition of lead. The ends of the shafts are also wider than normal, due, probably, to a chronic lead osteitis or osteopathy.

SPECIAL DIAGNOSTIC SIGNS AND TESTS

A lead line at the gum margins, characteristic of lead poisoning in adults, is dependent on the decomposition of food débris and the precipitation of lead sulphide particles in the capillaries of the gums. We were able to detect this line in very few of our cases and, therefore, do not consider it to be a reliable sign of lead poisoning in infants and children.

Basophilic stippling of the red blood corpuscles, if present to an appreciable degree, is of considerable diagnostic significance, although it is sometimes found in other conditions. It seems to be transient and may be absent even during the acute stage of severe lead poisoning.

Chemical analysis of excreta is advantageous in that minute amounts of lead may be detected. It has been shown, however, that under present-day living conditions practically all persons, young and old, are constantly excreting small amounts of the metal (7). Unless the analyses are quantitative, interpretation is difficult; the technic of this specialized procedure makes chemical examination available in only a limited number of laboratories.

With the spectroscopic analysis of blood

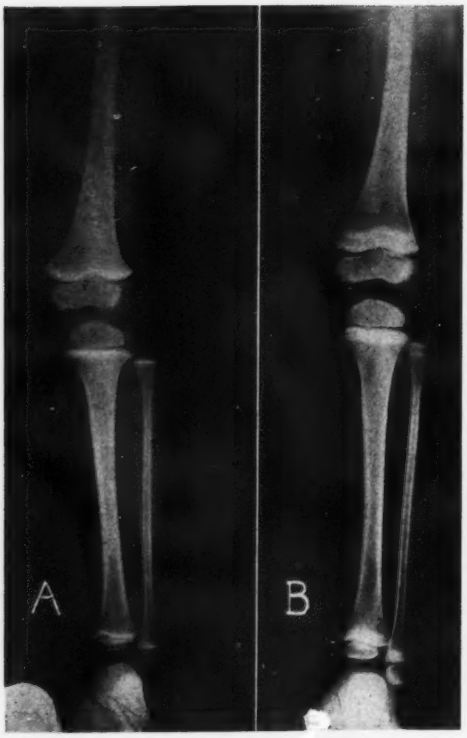

Fig. 4. L. H., aged 19 months, admitted on account of refusal to eat, irritability, and change of disposition. In a routine film of the chest the margins of the ribs were seen to be quite dense. Films of the extremities (*A*) were then obtained (Sept. 28, 1932) which showed the dense bands at the metaphyseal margins. Film (*B*), five months later (Feb. 21, 1933) shows the typical broadening of the lead line as the result of growth.

Fig. 5. P. S., aged 15 months. Not a case of lead poisoning. In (*A*), made June 27, 1931, the margins of the femur and tibia are quite dense, due to recent calcium deposit. It is not of the metallic density of lead. Film (*B*), four months later (Oct. 24, 1931), shows no appreciable change in the density or width of the bands at the metaphyseal margins, which is in contradistinction to the bands due to lead.

as advocated by Shipley, Scott, and Blumberg (12) we have had no experience.

ROENTGENOLOGIC FINDINGS

The roentgenologic findings appear to be among the most dependable diagnostic signs of lead poisoning in infants and children. The roentgen signs recognized independently by several observers (9, 13, 2, 6) consist chiefly in the finding of heavy bands of increased density at the growing ends of long bones or at the margins of flat bones.[2] With one possible exception these bands in the growing ends or margins of bones have been found in all of our cases of lead poisoning in children. The true bands of lead deposit are usually distinctive, having a metallic character which is comparable to that of the lead numerals used as markers on the edge of films. The depth of these opaque bands in the different bones appears to be proportional to the rate of growth, and, in general, the bands stand out most distinctly where growth is most rapid.

Contrast on the film depends largely on the amount of superimposed dense tissue and, therefore, the larger, rapidly growing areas of bones are best suited for the demonstration of lead bands. Pro-

[2] We have on a few occasions observed dense flecks of foreign material in abdominal films which were presumably paint in the intestines.

jection of the rays should be as nearly perpendicular to the end of the shaft of the bone as possible. By centering directly over the knees one has the advantage of visualizing the lower ends of the femora as well as the upper ends of the tibiæ in what are practically perpendicular planes.

The studies of Aub and his co-workers, demonstrating the tendency of lead to deposit in the bones of the body, suggest that the deposition of the roentgen-opaque metal in the growing portion of the bones is at least the chief cause for the appearance of the bands of increased density, observed on the films. That deposition of lead in the growing bone is actually the cause of these bands of increased density is indicated by the results of chemical analyses of the bones of fatal cases in which it has been demonstrated that lead is present in much heavier concentration at the growing margins than in other parts of the cortex, while the calcium content is actually diminished (Table I).

Park and his associates (10) found in histologic sections an unusual persistence of the framework of cartilaginous intercellular substance. They mention as a possible cause, a lowering of osteoblastic activity due to the action of lead on the tissues.

As gross evidence of what might be considered a lead osteitis or osteopathy one sees transverse lines or scars in the roentgenograms years after the ingestion of lead has ceased (Fig. 2). Chronic cases may show actual widening of the ends of the long bones where lead has been deposited over a prolonged period of time (Fig. 3).

Fig. 6. J. T., male, aged 17 months, was brought originally to the hospital on account of an injury. The history revealed that the child had a persistent habit of chewing paint off the furniture and woodwork. There were, however, no symptoms of lead poisoning. This was considered a case of latent plumbism, and the mother warned about the danger. Two weeks later the boy was brought back with discharging nose, fever, vomiting, and convulsions. The acute respiratory infection, with fever, was evidently the immediate cause for putting enough lead in circulation to bring on acute symptoms of lead intoxication.

Any difficulties we have had in the interpretation of films have been not so much in failure to detect the dense bands when lead was present, as in the differentiation between lead bands and those due to heavy calcium deposit. In healing or recently healed rickets, especially if Vitamin D in the form of viosterol has been administered, the metaphyseal margins may be very heavy. One should be cautious in making a diagnosis of plumbism if there is evidence of recently healed rickets. It must also be remembered that in normally growing infants the metaphyseal margins are sometimes fairly dense. Equivocal lines, in our experience, have usually not been due to lead. As a check on the accuracy of an original impression, one may re-examine the knees in the course of two or three months. If lead was present originally, the bands will have become broader, following the growth at the ends

of the bones (Fig. 4). On the other hand, if the bands originally were due to calcium deposit, they will not have broadened but will remain essentially the same as time goes on (Fig. 5).

Other causes of densities at the ends of the long bones have been mentioned in previous papers, but actually, their importance as a possible source of confusion is almost negligible. Zones of increased density formed following the administration of elementary phosphorus are an exception (11) and simulate closely the bands of lead deposit.

Occasionally bands typical of lead deposit are found in the bones of children with no symptoms of lead poisoning, who are examined for some other reason—for instance, an injury to the leg (Fig. 6). These usually represent cases of latent plumbism. It is important that such cases be recognized because these patients may at any time develop symptoms of acute lead poisoning.

TABLE I.—DETERMINATIONS OF LEAD AND CALCIUM IN THE CORTEX OF THE SHAFT OF THE FEMUR AND IN THE LEAD LINE AT THE GROWING END OF THE FEMUR.[3]

	Cortex of Femur	End of Femur
Mgm. Ca per gm. bone	209.0	83.5
Mgm. Pb per gm. bone	0.114	0.602
Mgm. Pb per gm. Ca	0.546	7.21

SUMMARY

Lead poisoning in children is a serious disease of relatively frequent occurrence, characterized in the more severe forms by an encephalitic process leading often to a fatal termination or to permanent cerebral injury in the patient.

Inasmuch as therapy directed toward relief of the encephalitic process is unsatisfactory, prevention of the ingestion of lead, and diagnosis of the disorder before the development of cerebral involvement are of the utmost importance.

The roentgen signs of lead poisoning are not specific, yet, through experience, we have learned that they are dependable and of the greatest value in differential diagnosis. By correlation of the clinical and roentgenologic findings, a diagnosis of lead poisoning usually can be arrived at with a high degree of certainty.

[3] Chemical analyses by Dr. L. T. Fairhall.

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THE EFFECT OF RADON IMPLANTS ON THE CYTOLOGY OF THE LIVER OF THE ALBINO RAT[1]

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RADIOTHERAPISTS, since the early days, have depended for therapeutic results on selectivity of their radioactive agent for certain cells of the organism. Since mature or fully differentiated tissue possesses increased resistance to irradiation, particularly to the hard beta and gamma rays of radium, the stages of cellular retrogression after exposure to these rays no doubt transpire more slowly in the adult, and thereby afford adequate time for a more accurate and comprehensive study of the consequent cellular changes.

This experimental study was undertaken to determine the cellular changes which occur in the liver, a specialized parenchymatous organ, subjected to the influence of radium as contained in gold-filtered radon seeds. The white rat was selected for the experiments because large numbers are available, and because the rat is well adapted to operative procedure and laboratory confinement.

In 1898, three years after the discovery of the roentgen ray, Curie submitted her thesis regarding the new element, radium. Investigations from the standpoint of its physical organization were first undertaken, and many of the then unknown physical characteristics of the new element have become more or less common knowledge. In 1911 Becton and Russ exposed pieces of fresh spleen, liver, pancreas, duodenum, and kidney to radium emanation in order to study the effect on Altmann's granules in the cytoplasm. They concluded that the alpha ray was chiefly responsible for the disappearance of these granules from the cell bodies. Richards showed that exposure of cells to rays of great intensity retarded or even inhibited growth, subsequent differentiation and regeneration, and even interfered with the processes of cell division. Amitosis was induced in instances in which formerly indirect cell division had been the method of multiplication. The degree of injury to the chromatin appeared to be an important factor.

In 1927 Russ and Scott reported their study of the effect of emanation on tumor and hepatic cells of rats. They concluded that the tissue remained practically unchanged if the intensity of the irradiation was below the rate of one beta particle each second. They also observed a definitely diminished effect of the irradiation on cells directly around blood vessels.

METHOD OF EXPERIMENT

All animals used were prepared surgically, and laparotomy was performed through a median line incision under ether anesthesia. The presenting left central lobe of the liver was held lightly in gauze and the radon seed was introduced about 0.5 cm. below the surface of the liver by means of a suitable spinal puncture needle with a well fitting obturator. The slight bleeding thus induced was easily controlled with warm moist gauze sponges, and the abdominal wound was sutured with linen. Operative procedures averaged approximately four minutes, thus making the amount of ether used practically negligible. In order to determine the effect induced within the liver by the mechanical irritation of these gold seeds, a number of animals was observed in which identical seeds, without the emanation, were introduced into the corresponding lobe of the liver. These animals served as controls.

The active radon seeds used were about 3 cm. long and 1 mm. in diameter; 0.3

[1] Submitted for publication Nov. 13, 1931.

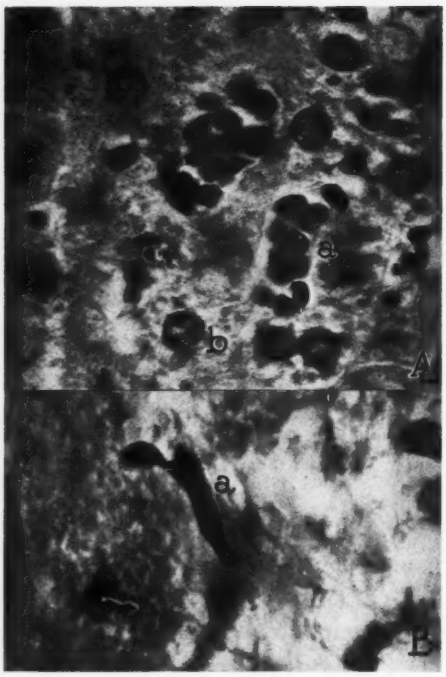

Fig. 1-*A* (*upper*). Nests of small round cells in hepatic sinusoids of irradiated liver twenty-four hours after operation; *a*, small round cells; *b*, hepatic cell (× 800).

Fig. 1-*B* (*lower*). *a*, histocyte in necrotic zone of irradiated liver forty-eight hours after operation (× 2,000).

mm. 14 carat gold composed the walls of the tiny cylinder. This 0.3 mm. of gold screening absorbs all but about 0.36 per cent of the beta rays and permits the passage of 82 per cent of the gamma irradiation (2). The total irradiation transmitted with this amount of filter is 3.16 per cent, and of this 8.8 per cent is beta and 91.2 per cent is gamma. (The original amount of unfiltered beta is much greater than gamma.)

The irradiated and control animals were killed by exsanguination at six, twelve, forty-eight and ninety-six hours, and seven, fourteen, thirty and sixty days following operation. At necropsy the lobe of the liver containing the radon seed was excised, and with a sharp blade it was cut into parallel sections about 2 mm. thick, fixed in formalin and stained with hematoxylin and eosin and van Gieson's stain. The silver carbonate method of Del Rio Hortega was also employed for a study of the reaction of the irradiation on the mitochondria.

The radon seeds for the six-hour series contained approximately 1.33 millicurie each; those for the twelve- and twenty-four-hour series, 0.5 millicurie each; those for the forty-eight-hour and four-day series, 1.1 millicurie each; those for the seven- and fourteen-day series, 1.5 millicurie each, and those for the thirty- and sixty-day series, 1.35 millicurie each. The seeds used for the control animals were valueless gold seeds but otherwise identical in every respect to those containing the active substance used for the irradiated animals.

OBSERVATIONS

At six hours following the operative procedures the reaction of the test animal to the radon seed was essentially identical to that of the control animal. A localized inflammatory reaction had taken place, and the local histocytes, or Kupffer cells, were markedly injured in the region immediately around the site of the implant. These cells in normal hepatic parenchyma are ordinarily spindle-shaped or star-shaped and they usually lie along the wall of the sinusoid or frequently are free in the blood stream. With hematoxylin stains the nuclei of the cells subjected to the irradiation were deeply colored, and they were often so large as almost to obscure their cytoplasmic bodies. In the regions immediately surrounding the site of implant, however, a differentiation in the staining reaction was manifest at six hours in that the cells stained lightly with hematoxylin. At twelve hours after operation these histocytes in the irradiated liver had increased, not only in size but in number in both the outer portions of the necrotic zone and in the sinusoids of the surrounding normal parenchyma of the liver.

At twenty-four hours after operation a marked contrast in the cytologic reaction

induced by the radon seed and the control seed was really first manifest. In the liver containing the active seed there was an acutely injured zone immediately around the seed, whereas a wider zone of slighter injury but of more chronic reaction lay just peripheral to it. From the slightly injured region the transition to normal hepatic parenchyma was very gradual. In marked contrast to this reaction there was a sharp or abrupt transition from the injured inflammatory zone to the normal parenchyma in the liver containing the inactive gold seed used as control. The sinusoids of the irradiated liver were engorged with erythrocytes and leukocytes, and there was an increase in the number of local histocytes. There was infiltration of small round lymphocytes and the arrangement of these many small cells was peculiar; there were groups or clusters of them in the normal tissue surrounding the necrotic zone (Fig. 1-*A*). At forty-eight hours after implantation excessive nuclear débris in fragmented cells were interspersed with many polymorphonuclear leukocytes around the site of the radon seed. At the outer border of a zone of lightly stained enucleate hepatic cells and many histocytes, there was a narrow irregular zone consisting of more deeply stained hepatic cells with pyknotic nuclei, small round cells and wandering histocytes. These lymphocytes and histocytes had further increased in number and the former continued to show the "nest" arrangement within the sinusoids more remote from the necrotic areas, whereas the latter appeared in a variety of forms in the deeper necrotic zone. The ratio of histocytes to the number of round cells decreased from the center to the periphery of the necrotic zone, and unusual nuclear patterns wherein small globules of chromatin were held as by a thread to the main nucleus (Fig. 1-*B*), were often encountered. Many of these cells were dumbbell-shaped, showing a faint protoplasmic connection between the two nuclear segments thereby indicating an amitotic cell division. It is difficult to describe in detail and exactness the multiplicity of the shapes and sizes which characterized these greatly enlarged wandering histocytes, but the lymphocytes in the so-called nests manifested a rather constant tendency toward an ovoid nuclear form.

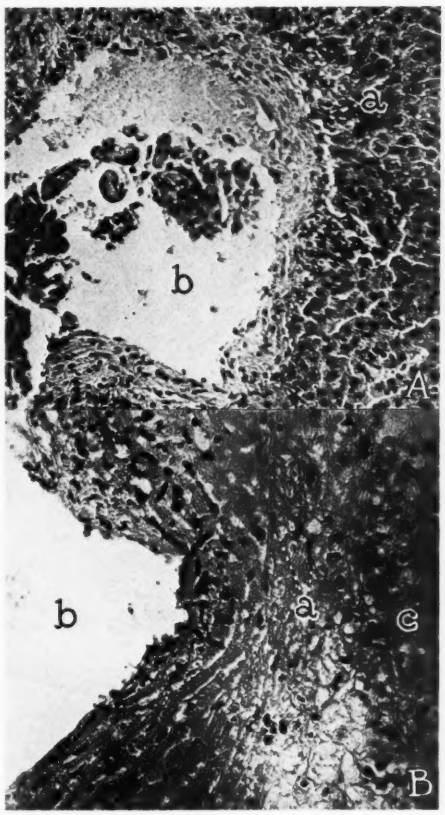

Fig. 2-*A* (*upper*). Hepatic lesion of control animal, seven days after implantation of inactive seed; *a*, normal parenchyma; *b*, site of inactive seed (× 190).

Fig. 2-*B* (*lower*). Hepatic lesion of animal seven days after implantation of active gold seed; *a*, migrating histocytes; *b*, site of active seed; *c*, necrotic parenchyma (× 190).

Hepatic cells closely associated with blood vessels in portal spaces appeared to be less affected by the emanation than those more remote (Fig. 2-*A*). Whether this is due to such proximity, thereby affording perhaps more adequate and rapid blood supply, cannot be definitely stated. In studies on toxic reactions in the liver

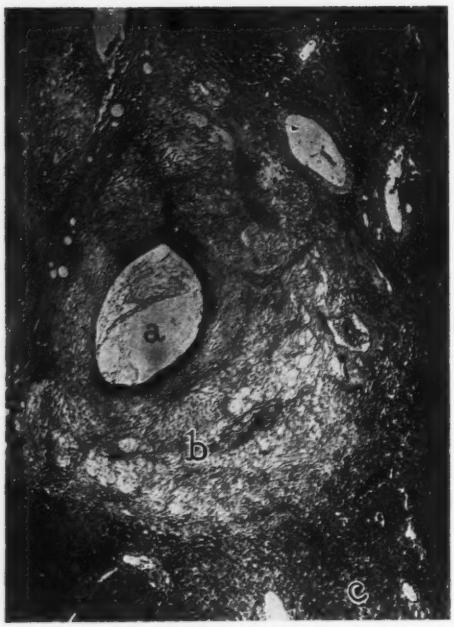

Fig. 3. Hepatic lesion of animal thirty days after implantation of active gold seed; *a*, site of active seed; *b*, reticular fibers; *c*, normal parenchyma (× 35).

we have noted, especially following poisoning by carbon tetrachloride, that cells immediately adjacent to blood vessels are far less likely to be injured than those in central or peripheral portions of the lobule.

Seven days after implantation of the active and control gold seeds into the hepatic parenchyma, further differential reactions had occurred. The liver subjected to the radium emanation of the gold seed appeared to be chronically inflamed, and the enucleate lightly stained hepatic cells maintained an arrangement essentially normal. The zone of injury, however, was extensive, and near its periphery connective tissue fibrils formed a loose network in which both lymphocytes and pyknotic cell nuclei were embedded. The lesion in the liver used as control, on the other hand, was far less extensive and there was an abrupt transition from the zone of inflammation to the peripheral normal parenchyma (Figs. 2-*B* and 3).

After fourteen days the reactions within the irradiated parenchyma were comparable to those noted, except that injury was greater. Bizarre types of histocytes were scattered rather widely through a wide zone of hyalinized necrotic tissue, but near the periphery of the lesion these reticular cells were more nearly normal in form. Often at the periphery of the lesion apparently normal cells of the parenchyma were scattered through the fibrillar network. Marked thickening of the walls and hyalinization of related blood vessels were observed for the first time in all livers subjected to the emanations.

On the thirtieth day apparently normal histocytes had penetrated the necrotic zone and were scattered in considerable numbers throughout the center of the lesion, whereas nearer the periphery they were infrequent. At the extreme edge of the lesion, the apparent limits of the effect of the emanation, histocytes had again assembled in considerable numbers. They were all now more nearly normal in shape and had lost the multilobular form noted during the earlier phases of the reactions. Nests or groups of small cells were present in the normal parenchyma just beyond the edge of the lesion, and it is not unlikely that these represented stages in the proliferation of the infiltrating reticular cells. Hyalinization of blood vessels initiated earlier, characterized the lesions at thirty days, for the medial and intimal layers were completely congealed. The fibrous adventitial coat, on the other hand, continued to show some resemblance to the normal condition. There was no definitely circumscribed fibrous capsule, such as is often encountered in other reactions, for the reticular tissue of the hyalinized area continued without marked gradation into normal parenchyma. Although some of the experimental animals were observed for sixty days, the extent of injury at this time was most comparable to that described at the thirty-day interval. Further increase in the number of local histocytes was perhaps most noticeable and was in marked con-

trast to the number identified in the lobes of the liver containing the control or blank seed. A further striking contrast between the control and active radon seeds concerned the nature of the tissue delimiting the lesion from normal liver. A fibrous capsule was laid down around the lesion induced by the inactive foreign body and formed a definite wall which separated the necrotic from the normal tissue. In the hepatic tissue subjected to emanation no such capsule was formed; the necrotic hyalinized tissue continued more or less imperceptibly into the more distal normal functioning parenchyma.

COMMENT

The most marked cellular reaction induced by the emanation of the radon implant in the liver was demonstrated by the local histocytes. These cells, originally described by von Kupffer, and often so designated, are a part of the defense mechanism in the body. They are probably not derived from vascular endothelium but have an origin comparable to the other wandering phagocytic cells of the animal organism and thus may well be designated as the histocytes of the liver.

The initial response to the emanation, first demonstrated at twelve hours following operation, consisted in a marked increase in the number of these phagocytic cells throughout the area immediately surrounding the radon implant, as well as in the more remote hepatic parenchyma. The early reaction appeared to be stimulative, when all or many of the local histocytes in a given region became detached from their position along the sinusoid and migrated toward the source of the emanation. Coupled with an increase in size these wandering cells often assumed unusual shapes or outlines rarely if ever encountered in a normal lobule of the liver.

The source of so great an increase in these cells is not demonstrated. It is hardly supposed that they arise from preexisting histocytes, for evidence of cell division is not common. Nuclear budding or a process in which a portion of the nucleus was constricted and separated from the parent cell was occasionally seen; it may be that amitotic division was employed to secure such rapid proliferation.

With this rapid early increase in histocytes there was infiltration and proliferation of small, round lymphocytes. These cells often appeared in groups or small nests, and there were indications that they arose from some pre-existing littoral cell along the sinusoid. These nests were more abundant in the peripheral portions of the lesion where the histocytes were less common and thus there was evidence to indicate some ontogenetic identity between the histocytes and the lymphocytes. In the absence of the spleen it has been shown that these littoral histocytes give rise to similar nests of small round cells, comparable to those encountered in this study of the effects of the emanation.

Less than twenty-four hours after operation, the differential reaction in the control livers, and in the irradiated livers, is largely one of degree and not of kind. The reaction to the inactive gold seed used as control was such as any foreign body would induce. Migration of histocytes and the formation of fibrous tissue with the development of a demarcating wall ensued, so that the extent of injury to the liver was largely determined at that time. The arrangement of hepatic cells into typical cords or strands persisted in both the control and the irradiated parenchymas. Although these cords were most atrophic, largely enucleate and reacted but lightly to the eosin stain, they retained their lobular arrangement longer in the livers irradiated than in those containing inactive seeds.

The extent of injury induced within the irradiated parenchyma increased, and at seven days a chronic inflammatory reaction had been induced, vastly more extensive than that in the control animal. At fourteen days the lesion was even more extensive and for the first time changes in the vascular channels were noted. Both

intimal and medial walls of the blood vessels in the portal spaces had become thickened, and hyalinization had occurred in many instances. Since these changes in the blood vessels were noted so long after pathologic conditions were induced in the parenchyma, it would appear that the lesion was not related to an altered blood supply. Proximity to the vascular channels of the blood appeared to protect hepatic cells from injury comparable to that sustained by other cells, as hitherto shown by Russ and Scott. In many instances normal hepatic cells adjacent to blood vessels in portal spaces were flanked by cells in various stages of degeneration induced by the emanation.

SUMMARY

Gold filtered radon seeds were implanted in the livers of albino rats and histologic study made of the irradiated tissue at periods varying from six hours to sixty days. A series of rats, in which inactive but otherwise identical gold seeds were implanted into corresponding portions of hepatic parenchyma, served as control animals and were killed at like intervals after operation.

The most marked cellular activity in the liver was demonstrated by the local histocyte. An increase in number and in size was noted at twelve hours and the maximal activity was attained at forty-eight hours. There was definite evidence of amitotic cell division by fragmentation and budding.

A latent period of twenty-four hours after implantation of the radon seed was noted in advance of any definite cellular injury, due to irradiation.

Hepatic cells about interlobular blood vessels repeatedly exhibited less effect from the emanation than those in the intralobular parenchyma.

Marked increase in the amount and more definite diffusion of the connective tissue fibers were present in the irradiated sections after seven days, and hyalinization of blood vessels was first present at fourteen days.

There was definite retention of the general form and shape of the cell cords of the parenchyma up to seven days. Subsequently, however, the area became hyalinized so that at fourteen days, large hyaline areas surrounded by radiating and diffuse connective tissue fibers characterized the lesion.

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IRRADIATION AND ELECTROSURGERY IN THE MANAGEMENT OF CARCINOMA OF THE URINARY BLADDER[1]

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INTRODUCTION

THE treatment of carcinoma of the urinary bladder with radium, roentgen rays, and electrosurgery is not new. Considerable experience along these lines during the past 17 years has taught me that it is generally best to begin treatment with thorough external roentgen irradiation, followed promptly with the indicated surgical procedure and irradiation within the bladder with radium element. Treatment is completed with active post-operative external roentgen irradiation.

Preliminary or Pre-operative Roentgen Therapy.—Regardless of the type or location of the carcinoma within the bladder, treatment almost always begins with thorough roentgen irradiation. These treatments are so planned that they will be completed within two weeks' time, with not more than eight to ten days actually consumed in the treatments. The number of ports of entry varies from four to seven according to the size of the patient's pelvis. They are taken from the lower abdominal region, the sacro-gluteal region, from the lateral aspects of the pelvis, and from the perineum. Generally in this two weeks of preliminary roentgen treatment each port is treated twice with rays generated by valve tube machines with condensers and constant potential at 190,000 volts, the focus-skin distance being 50 cm., the filter 0.75 mm. Cu plus 3 mm. Al, 37 per cent of such rays reaching a depth of 10 centimeters. The number of ports of entry, taken together with the time duration of the treatment over each, is so planned that not less than 750 r units dosage will actually be delivered to the diseased bladder by the total irradiation from all ports. The second series of pre-operative roentgen-ray treatments is given in exactly the same way, thus bringing the total dosage up to 1,500 r units.

Clinical Results of Pre-operative Irradiation.—Frequently following preliminary roentgen irradiation there is marked improvement in the patient's general condition, especially in cases suffering with severe hemorrhage and secondary infection. Bleeding is controlled, often within 24 hours after treatment is begun. Aside from the benefit that the patient experiences from this alone, is the fact that further cystoscopic studies can be made much more valuable because the vision of the examiner is not clouded with blood, and he is, therefore, able better to define the extent of the involvement. Urinary sediment, pus cells, and débris, *i.e.*, products of a chronic infection, lessen and in some cases entirely disappear. Because of this the temperature is lowered and will sometimes reach normal within a few days or before preliminary treatment is completed. In a considerable percentage of cases there will appear multiple implantations in the wall of the bladder following operation. Preliminary irradiation reduces these to a minimum because irradiated cancer cells either do not grow at all when transplanted or grow with difficulty. Furthermore, while giving these treatments, sufficient time passes to permit of careful study and treatment of the patient's other vital organs; it is felt, therefore, that no valuable time has been lost or wasted

[1] Read before the American Congress of Radiology, at Chicago, Sept. 25–30, 1933.

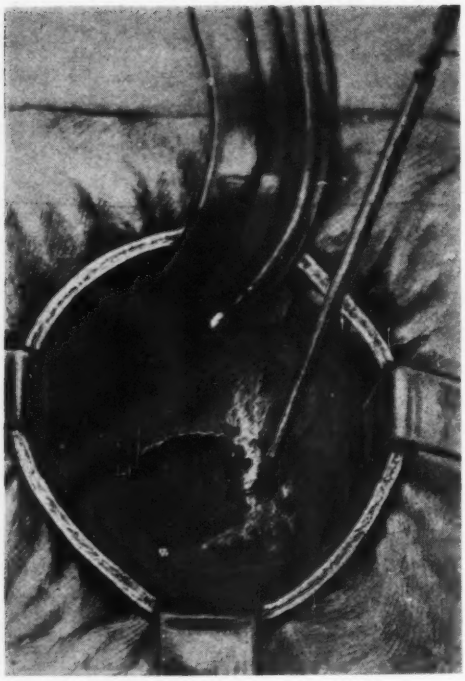

Fig. 1. Electrothermic coagulation of tumor within the bladder by means of a suprapubic cystotomy. (*Pfahler and Thomas.*)

because of this preliminary or pre-operative roentgen irradiation.

Electrosurgery.—There are several reasons why all attempts to remove or destroy a carcinoma of the bladder should be made by means of a suprapubic cystotomy. The first and most important reason is that it is not always possible to combine an expert cystoscopist and electrosurgeon in one and the same man. There is a certain mortality that seems to follow this operation, but this is more than offset by the thorough work that is possible by cystotomy. Frequently the expert cystoscopist reports that he is not sure whether or not the bladder wall is infiltrated or where diseased bladder wall meets healthy tissue. Blood and smoke during attempts to destroy carcinoma of the bladder through a cystoscope add so much more to the difficulties that no one can ever be sure that all of the disease has been removed or destroyed. All of us are familiar with the poor results which follow removal of only a portion of the carcinoma, also the fact that complete removal or destruction at one sitting is better than complete removal or destruction by many sittings insofar at least as ultimate results are concerned. Therefore, if good results are to be expected, even in the simplest cases, which naturally are expected to give the highest percentage of permanent results, nothing short of thorough, complete electrosurgery by means of a suprapubic cystotomy is advisable.

Malignant Papilloma.—Since this type of lesion does not typically involve the bladder wall it is a simple matter to destroy the entire growth at one sitting by means of the hot bipolar current, *i.e.*, by electrothermic coagulation. By using a milder, more superficial, current it is well to extend the destruction of tissue by coagulation around the base of the mass upon the bladder wall in what is undoubtedly healthy, normal tissue.

Papillary and Infiltrating Carcinoma.—In many cases in these groups it is difficult to decide just which electrosurgical procedure is apt to be followed by the best result. The selection of a definite method depends upon the extent of the disease, whether it is limited to the bladder wall or extends to structures outside the bladder. Also, the location of the growth within the bladder has a great deal to do with the final decision. If the growth is limited to the bladder, without extensions, providing it is located in the vertex, the anterior or the posterior vesical walls, good results often follow resection. However, none but a radical operation is of value, for which operation, of course, the bipolar, cutting, high frequency current is used. If the tumor involves tissues or organs outside the bladder wall, or localized tumors located at the prostatic orifice or trigone, or carcinoma of the posterior trigone involving a ureteral orifice, best results will no doubt follow destruction of the mass as completely as possible by electrothermic coagulation followed by radium treatment. Great care must be exercised here because

Fig. 2. Radium needles placed in base of tumor following electrothermic coagulation and removal of the tumor. (*Pfahler and Thomas.*)

Fig. 3. Sagittal section, radium needles in place with their threads passed through drainage tube. (*Pfahler and Thomas.*)

it is perfectly possible to destroy the rectum, even though a finger is inserted into it during the operation. Since only palliation is expected to follow in the vast majority of these hopelessly advanced cases, in many instances best results will naturally follow a thorough coagulation of only that portion of the tumor projecting above the bladder wall, followed by radium therapy, or intense, highly filtered roentgen-ray treatment. There is much evidence from many sources that roentgen therapy with modern dosage technic will supplant all other methods of treatment, particularly for the advanced cases.

RADIUM THERAPY

Radium therapy is indicated in all three groups of carcinoma of the urinary bladder. When used following roentgen-therapy as outlined above, total radium dosage can be reduced, thereby eliminating troublesome reaction in the bladder. However, the actual dosage applied in specific instances is determined by the size of the mass plus the extent of the involvement; therefore, for malignant papilloma the dose varies from one-half to one gram-hour for a single small tumor. For multiple lesions involving large portions of the bladder wall, radium treatment from a central location is indicated. This is done by placing the applicator in the center of a plain gauze packing which fills the bladder. With an equal distance to any portion of the bladder wall of 2 cm. through the gauze, the dosage ranges from 1.5 to 2.5 gram-hours.

Papillary and infiltrating carcinoma may be treated by either one of two methods: the implantation of radium element needles into the coagulated base or residue, as the case may be, or the packing of heavily filtered capsules against the base of the mass. The radium element needling

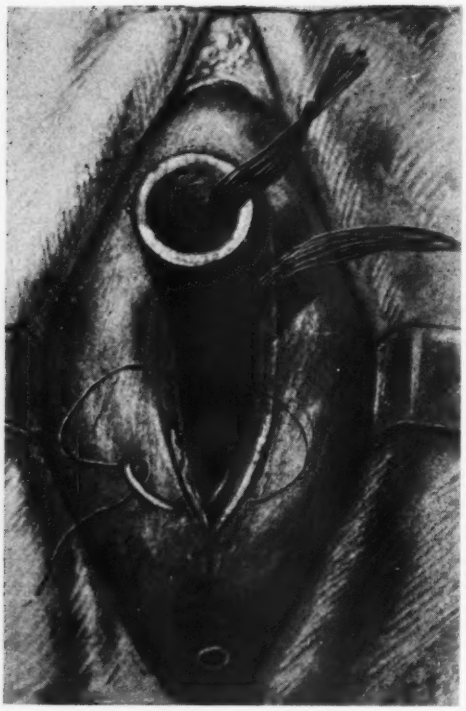

Fig. 4. Closure of bladder showing placement of drainage tubes and threads to radium needles. (*Pfahler and Thomas.*)

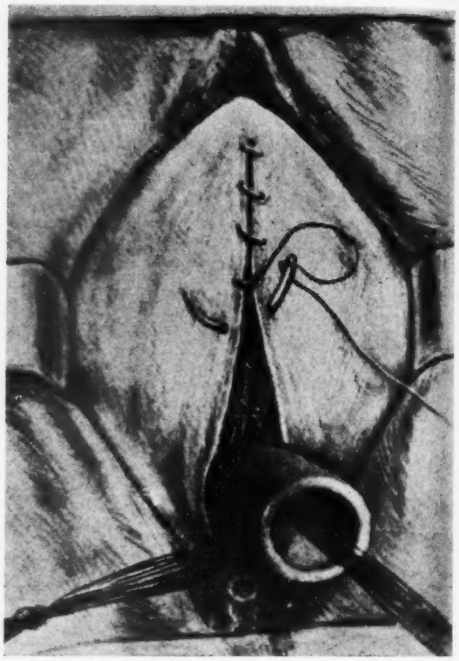

Fig. 5. Bladder rotated downward by drainage tube which is fixed by stitches through lower angle of skin incision. Recti muscles and fascia are being closed. (*Pfahler and Thomas.*)

method of treatment is the older, has been used in many clinics in both this country and abroad, and is perhaps, therefore, a more standardized method of treatment. It is best done with platinum needles containing from one to two milligrams of the element. A sufficient number of needles must be at hand so that one may be buried into each cubic centimeter of coagulated base or tumor residue. These needles are left in place until the indicated dosage has been administered.

A newer method of post-coagulation radium therapy, a method that appears thus far to have great possibilities for the future, is by the use of extremely heavy filters, even up to as much as four millimeters of lead. This treatment is carried out by placing the radium element capsules within the filters and packing them against the coagulated mass. This method has for its object the production of a pure gamma-ray irradiation of extremely short wave length. Too few cases have been treated by this method and the elapsed time is too short for me personally to draw any conclusions as to the permanency of results. However, a detailed report is promised from Dr. Pfahler upon this method of treatment which will, of course, prove the true value of this method of radium treatment.

POST-OPERATIVE AND RADIUM THERAPY

In from three to eight weeks following the completion of radium treatment not less than two further series of roentgen-ray treatments are given in exactly the same manner as described above. These bring the total roentgen dosage up to 3,000 r without, at any one treatment, producing an erythema. The skin is, however, deeply tanned by such dosage.

With such a combination of roentgen and radium treatments it is felt that the disease is kept saturated with radiations to the point of toleration for a considerable period of time; in fact, that the treatment given is probably as thorough as is applied by any one.

RESULTS

In 1922 Barringer reported 43 per cent three-year recoveries in papillary carcinoma upon which a pathologic diagnosis had been made, together with 29.7 per cent of the infiltrating type. There were 98 cases in this group. Cases to the number of 127 were treated without a microscopic diagnosis, with 55 per cent three-year recoveries in those of the papillary group and 27.8 per cent recoveries in the infiltrating type.

In 1926 Burnam reported 11 cures, *i.e.*, 9.9 per cent out of 111 cases of large carcinoma, and 20 (35 per cent) cures of a group of small carcinomas. There were 59 cases of large papillary inoperable cancer, with 7 cures (12 per cent), and 20 cases with palliation. There were 29 cases with what were classed as small and medium papillary carcinomas, with 9 (31 per cent) cures. The 49 cases of large, inoperable, infiltrating carcinoma gave 4 (8 per cent) cures, and 13 cases of palliation. Of 9 cases with small and medium infiltrating carcinoma, there were 5 (55 per cent) cures and 4 cases of palliation.

In 1931 Pfahler presented a remarkable report based upon the treatment of 83 cases of advanced, large, inoperable carcinoma. In this group of hopeless cases, 15.3 per cent were well at the end of five years. It is impossible to overestimate the value of this report because such results followed the treatment of cases in which palliation was all that could be expected. The quality of this work and the value of this report are at once appreciated when one considers the results of surgical treatment in carcinoma of the bladder, the results of surgery upon early, localized, hopeful cases. Lower, for instance, reports only 7 per cent five-year cures.

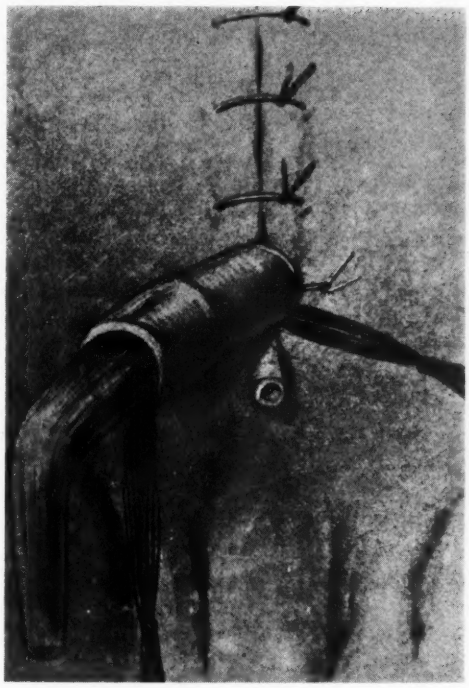

Fig. 6. Skin sutured showing drainage tubes and threads to radium needles. (*Pfahler and Thomas.*)

In my clinics, prior to 1928, there were treated 63 cases with a pathologic diagnosis, upon which I have a five-year follow-up. Of these, eight were single malignant papilloma, of which five (62.4 per cent) recovered. Two patients with multiple malignant papilloma died, but previously good palliation was noted in both instances. Two, of six cases with small and medium sized papillary carcinomas, recovered, and in two other cases excellent palliation followed treatment. In this group of 63, there were 11 cases with large, inoperable cancer, of which two recovered, while four experienced good palliation. Of 36 cases of the infiltrating type, four were small and medium, and of these, two recovered, while excellent palliation followed in the other two. Of 32 cases with large and inoperable cancer, four recovered, while good palliation followed in nine cases. Of the 11 cases with large, inoperable, papillary carcinoma and

the 32 cases with large, inoperable, infiltrating carcinoma, a total of six recovered.

CONCLUSIONS

1. The value of preliminary or preoperative roentgen irradiation in the management of carcinoma of the urinary bladder is stated, also the dosage.

2. Intravesicular operative procedures, together with irradiation with radium element in the form of needles and packs, are mentioned and briefly described. The radium dosage is also stated.

3. Post-radium or post-operative roentgen irradiation is advised and the dosage is stated.

4. The results of the treatment of carcinoma of the urinary bladder with irradiation and electrosurgery, as stated by several authorities, are included, and the paper ends with statistics from the writer's own practice covering 63 treated cases with a five-year follow-up.

55 Park St.,
Montclair, N. J.

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CASE REPORTS

REPORT ON X-RAY TREATMENTS IN GAS GANGRENE CASES

By J. J. FAUST, M.D., *Decatur, Illinois*

Since reading a preliminary report on the successful treatment of six gas gangrene cases by Dr. Kelly,[1] and knowing of the response to x-ray therapy in some cases of carbuncle and localized infection, the writer has had the opportunity to observe and treat five gas gangrene cases, with satisfactory results in each instance. They are reported herewith to corroborate the findings.

The technic of treatment was: 5-inch spark gap, 5 ma., 40 cm. distance from target to skin, with 0.5 mm. aluminum as a filter, for three minutes over each area. This therapy is such that it may be given with most portable machines and hence be available in many small institutions where radiographic work only is ordinarily done.

The number of cases reported is not large, but the importance of the condition and the splendid results so far obtained make one feel that the information should be passed on for what it may be worth in other cases. Further study and some changes in technic of treatment may be developed as other cases are encountered.

An explanation of the action of the x-ray is not definite. Recently three Stanford University zoologists have reported that x-rays played upon nutrient fluids are deadly to protozoa by producing small quantities of hydrogen peroxide The presence of the hydrogen peroxide would be fatal to these anærobic organisms. Due to the absorption of the hydrogen peroxide the x-ray treatments need to be frequent to produce more of the gas. This is what was found to be necessary in some of these cases.

Case 1. Male, age 15, while attempting to climb on a tractor fell underneath the plow which it was pulling, resulting in a compound fracture of the right leg. Three days later a cast was applied and sutures made while the temperature was 102° F. The next day the temperature had risen to 103.6°, and gas was seen in the tissues and on the radiograph. A culture was positive for *B. welchii*. X-ray treatments and serum injections were instituted and the temperature dropped a little. After eight treatments, no gas was seen in the tissues and the temperature stayed below 100° F. This temperature was due to the presence of other infection. The patient left the hospital at the end of the eighth week, and is now walking with the aid of crutches, and his leg has been saved.

Case 2. Mrs. H., aged 66, entered the hospital in severe shock, with multiple lacerations on the left forearm, involving the superficial circulation, tendons, and nerves, as well as the muscles from the wrist to the elbow, due to an accident. The pulse was poor and the prognosis bad. The next day the left arm was amputated six inches below the shoulder because of gangrene, multiple lacerations of the arm and forearm, and fractures. The pectoral muscles on the chest were also involved. The temperature was 105.6° F. A culture was positive for gas bacilli and gas bacillus serum was given. Ten x-ray treatments were given in six days' time and the temperature dropped to 99.8° F. Six and one-half weeks later the patient was discharged with the stump of the arm healed.

Case 3. Mr. L., aged 72, was in an automobile accident and the skin on the forearm was slipped back six inches, the triceps muscle was lacerated, and the ulnar and radial nerves were exposed. A culture was positive for gas bacilli, and serum was administered twice. Six x-ray treatments were given. The patient was discharged after two weeks' hospitalization.

Case 4. Male, aged 20, was gored by a bull, resulting in a ten-inch laceration across the abdomen through the skin, subcutaneous tissues, and the right rectus muscle down to but not involving the peritoneum. The wound had hair, leaves, and other débris in it. There was also a four-inch laceration in the left axilla, with hair in it. The wounds were cleansed, muscles and fascia were sutured, and a rubber drain was placed in position. Gas in the tissues and crepitus were noted twenty-four hours later. Serum was given twice. Eight x-ray treatments on the right side were given, and the wound appeared almost well. Six days later gas and crepitus developed on the left side, which had not been radiated. Three x-ray treatments to this area, with no serum, were sufficient. The patient was discharged as well ten days later.

Case 5. Female, aged 21, had an appendectomy, bilateral salpingectomy, and right oophorectomy by the same surgeon who treated Case 4, above, the same morning. Since she was dressed in the wards by the same nurse after the operation, the direct means of the infection is unknown, but three days after the operation she had a foul-smelling discharge from the incision. A culture for gas bacillus was positive. One dose of serum was given. Eight x-ray treatments were given in four days

[1] Kelly, James F.: The X-ray as an Aid in the Treatment of Gas Gangrene. RADIOLOGY, April, 1933, XX, 296-302.

and the discharge and odor stopped. The patient was discharged on the twenty-first post-operative day as well.

CONCLUSIONS

1. All patients recovered whether the wound was in an extremity or not.
2. The x-ray treatment was a definite aid to recovery.
3. The serum used was supposed to be specific for *B. welchii* and *B. vibrion septique*, whereas two cases had *B. clostridium tertium* infections. Since the serum was not positive for this organism it may not have had anything to do with the results and the x-ray may have been entirely responsible for the cures.

COMMENT

Should new cases be found, we may attempt early treatment with x-ray alone and use the serum only if results are not favorable in a reasonable time.

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BOOK REVIEWS

GRUNDLAGEN UND PRAXIS DER RÖNTGENSTRAHLEN-DOSIERUNG: DOSISMESSUNG UND DOSISFESTSETZUNG. By PROF. DR. MED. H. HOLTHUSEN, Leitender oberarzt am Allgem., Krankenhaus St. Georg, Hamburg, and DR. MED. R. BRAUN, Assistent am Strahleninstitut des Allgem., Krankenhause St. Georg, Hamburg. A volume of 249 pages, with 152 figures and 27 tables in the text and a supplementary phrenaphane scale. Georg Thieme, Leipzig, 1933. Paper: price, M. 18; bound, M. 19.60.

The adoption of the international roentgen has done much to unify x-ray treatment in that it permits standardization and comparison of dosage. In the formulation of this dosage unit Holthusen has been an active participant. In the past there have come from his institute many studies of the interrelationship of the physical and biologic factors which go to make up a roentgen effect. These studies have been amplified in the present book in an attempt to clarify some of the puzzling mechanisms concerned in the effects of varying doses of x-ray acting on the body and with the effects of the same dose under different conditions. Throughout the exposition the necessity for exactitude in the precise determination of a dose of x-rays is emphasized. The authors' first concern is with the physical aspects of dosage determinations (pages 1–84), and in this section they have written a thorough and, in fact, rather exhaustive consideration of the determination of quality and quantity of a "dose," presenting their material from the point of view of the physician rather than from that of the physicist. The second portion of the book (pages 85–245) takes up the practical applications of the relationships between physical and biologic effects. Of particular interest is the discussion of the actual measurement and administration of a predetermined dose of x-rays. In this connection the practical hints given by the authors for the solution of some common problems are well presented. The contents of this extremely well planned and executed book should be thoroughly understood by all roentgentherapists. The authors deserve great credit for such a lucid presentation of a complicated subject.

THERAPEUTIC USES OF INFRA-RED RAYS. By W. ANNANDALE TROUP, M.C., M.B., Ch.B. (St. And.), Honorary Consulting Electrotherapist to the Portman Hospital, Blandford; Honorary Physician to the Association of Retired Naval Officers; Member of the Honorary Advisory Editorial Board of "The British Journal of Physical Medicine"; Member of the Royal Institution. With Foreword by SIR WILLIAM WILLCOX, K.C.I.E., C.B., C.M.G., M.D., F.R.C.P. Second Edition. A volume of 90 pages and 18 plates. Published by the Actinic Press, Ltd., London, 1933. Price, 6 shillings and 6 pence.

The second edition of this book became necessary three years after the first publication, which shows that the medical profession is interested in this subject. The author, who has written other books on radiation (Ultra-violet Rays in General Practice; The Titanium Alloy Arc), assumes a conservative

attitude throughout the text. He discusses first the various sources of infra-red rays, methods for detection, and indications for treatment. This is followed by an outline of the technic. The combined use of infra-red rays and ultra-violet rays is recommended in certain conditions, particularly if a "cold source" of ultra-violet rays is used. The application and value of infra-red therapy in the relief of acutely painful conditions, rheumatism and allied diseases, rheumatoid arthritis, paresis, sprains, and long-standing injuries are briefly discussed and case histories are frequently quoted. Illustrations of the apparatus used in infra-red therapy are shown as well as some demonstrations of the technic of treatment. In an appendix the recently developed "long distance photography" by infra-red rays is briefly mentioned and a few examples of its accomplishments shown.

NEUROFIBROMATOSE. By PROF. DR. ROBERT KIENBÖCK and DR. HUGO RÖSLER, Vienna. Fortschritte a. d. Geb. d. Röntgenstrahlen, Ergänzungsband 42. A monograph of 52 pages and 21 illustrations. Published by Georg Thieme, Leipzig, 1932. Price, 9.80 marks.

The paper deals with tumors of nerves, five of which were examined after operation and six others followed up in the hospital. Besides these, Kienböck makes a critical examination of cases reported in the literature.

There are several varieties of tumors, the common type being multiple generalized neurofibromatosis, with tumors in nearly every organ. The large intrathoracic tumors, most of which are solitary and located in the posterior portion of the thorax, are of special interest. They are regular, egg-shaped, with smooth surfaces and have the appearance of cysts. They are distinctly seen in ordinary x-ray examination of the chest and are discovered not infrequently as incidental findings. They cause but few symptoms, are usually located posteriorly in the apical region, but may be found at the hilum. They do not pulsate. Deviation of the mediastinum is found only in the presence of very large tumors. Diaphragmatic paralysis from pressure is a rare finding.

The diagnosis of neurofibromatosis must be thought of, but can be made conclusively only if there are additional signs, namely, typical lesions of the skin and cord symptoms, psychic disturbances, or constitutional defects. Until now, these tumors have been diagnosed as sarcomas or dermoid or echinococcus cysts.

Similar tumors of nerves are found in various organs, sometimes also in the bones. The tumors found in the skin resemble pigmented warts. A secondary malignant degeneration may take place locally but metastases do not take place. Another type of nerve tumor is the ganglioneuroma. This is mostly solitary, of large size, and benign. Such tumors are also found in the posterior part of the thorax, but never accompanied by skin changes. Operation is indicated, but only to prevent local pressure.

W. HERBERT MCGUFFIN, M.D.

President of the Radiological Society of North America

OUR PRESIDENT

In this issue appears a portrait of Dr. W. Herbert McGuffin, M.D., who took office as President of the Society at the joint meeting of September last. Dr. McGuffin has a wide acquaintance in the Society, of which he has been a member since 1921. Although he lives in the far Northwest, he attends all of the Annual Meetings and keeps in close touch with the development of the Society. His ideals for the Society have been high, and his work has ever been constructive. Socially, Dr. McGuffin is immensely popular, and his has been a strong binding force in the upbuilding of our group.

Now, on the threshold of his year of executive leadership, RADIOLOGY extends to him warm congratulations on his record, and good wishes for the success of his administration.

EDITORIAL

LEON J. MENVILLE, M.D., *Editor* HOWARD P. DOUB, M.D., *Associate Editor*

RADIOLOGY—ITS RELATION TO MEDICINE

Roentgen rays, or the x-rays, at their discovery only thirty-eight years ago, were looked upon by the medical profession as a scientific revelation that would enable a surgeon to study a broken bone, or to locate a needle or a nail that was buried in tissue. These rays exhibited a curious phenomenon that might be of value in the practice of surgery. How could they be utilized? Doctors were curious, but conservative.

Ingenious instrument-makers invented machines; mechanical minds were discovered among the profession itself; but this new force was recognized by doctors only to the extent of its photographic value in revealing foreign elements in various parts of the body. Early tragedies which occurred in the handling of this novel agency called attention to an additional power within the roentgen rays. Scientists studied the phenomenon. If x-rays destroyed healthy tissue, why, some thinkers suggested, could they not also destroy cancerous neoplasms? Roentgenology was developed; a new science was born.

Three years after Wilhelm Konrad Roentgen discovered x-rays, Pierre and Marie Curie discovered radium. But another three years passed before the action of radium on human tissue, and its value as a therapeutic agent, became known—when Professor Bacquerel, of Paris, unwarily carried a tube of radium in his waistcoat pocket and suffered a severe skin burn.

Through careful study of the radio-active properties of these two agencies, the science of radiology was established.

Roentgenology and radiology had been born; and physicians and surgeons—first the radicals and soon also the conservatives—were not slow to hail them as valuable diagnostic and therapeutic agencies.

From the very beginning, the clinical use of radium and the therapeutic employment of the x-rays have been in the hands of licensed physicians; and although a few laymen were prominent in the purely technical or manipulatory phase of diagnostic roentgenology, the development of both the technic and the clinical application was the fruit of the enthusiastic and unselfish, even limb- and life-endangering, industrious labor of physicians. These physician-radiologists have laid their needs, and sometimes even the engineering plans, before the manufacturers, with the result that the latter have constantly devised improvements in equipment. It is a fact that most of the apparatus has been manufactured as a direct response to the expression of needs or problems by physicians practising radiology.

This new science, which has been universally accepted by the medical profession because of its valuable diagnostic and therapeutic powers, now claims the attention of organized medicine for unqualified recognition as an important specialty. Indeed, a large measure of recognition has already been given, as there is a section on radiology in the American Medical Association and in many of the constituent state associations.

But a diagnostic and therapeutic field in which recognized physicians only should have a place has been invaded by laymen and unscrupulous practitioners of the healing art. The profession of medicine finds itself confronted with the responsibility of deciding who of those administering these new agents are worthy of recognition in the new specialty.

In my opinion, recognition as specialists in a branch of medicine contemplates that the claimants shall present acceptable evidence, individually or collectively, that they are full graduates in scientific medicine of recognized medical schools, and that they are legally licensed to practise scientific medicine in their respective communities. In other words, the radiological specialist should be a physician who has at least the above qualifications.

Fortunately, the importance of this course is already recognized by those who have done so much to develop radiology and roentgenology, as this meeting indicates. To warrant recognition as specialists they realize that they must be graduates in medicine and scientifically trained physicians. Individuals who possess such qualifications already have the right to interpret their own findings and to an-

nounce their diagnoses. Others who do not possess such qualifications may act as valuable aids or associates under the guidance of qualified doctors, but naturally they cannot anticipate recognition as members of a specialty in medicine.

When one reflects on the great value of roentgenology and radiology as diagnostic and therapeutic aids in the practice of medicine and surgery, it is inevitable that their followers should quality as acceptable specialists of medicine. This fact is emphasized as we view this group of eminent men and their accomplishments.

Conspicuous proof of the general recognition of the value of radiology and roentgenology was recorded in the histories of the 8,840 cases of cancer cures of five years or more that were reported in October, 1932, by the American College of Surgeons. In 18 per cent of these cases, these therapeutic measures were the only remedy used, and in an additional 10 per cent they were used as supplementary forms of treatment.

This year's report of cancer cures recorded by the American College of Surgeons, we have reason to predict, will show the same encouraging results.

FRANKLIN H. MARTIN, M.D., D.Sc., *Chicago*
Director General, American College of Surgeons

COMMUNICATIONS

LETTER CONCERNING "THE VALUE OF A MULTI-PERFORATED SCREEN IN DEEP X-RAY THERAPY"

By F. LIBESON, M.D., "RADIOLOGY," MARCH, 1933, XX, 186.

In the issue of RADIOLOGY as indicated above, Liberson has made "A Preliminary Report on a New Method of Delivering Multiple Erythema Doses without Permanent Injury to the Skin." The thought and the method are not new. I described practically the same method in 1909. This was published in the "Journal de Radiologie" (de la Société Belge de Radiologie), Tome 3, page 185, in the French language, and shortly thereafter in the German language, in the "Fortschritte auf dem Gebiete der Röntgenstrahlen." The title was "Theorie einer Methode, bisher unmöglich anwendbar hohe Dosen Röntgenstrahlen in der Tiefe des Gewebes zur Therapeutischen Wirksamkeit zu Bringen ohne schwere Schädigung des Patienten, zugleich eine Methode des Schutzes gegen Röntgenverbrennungen überhaupt" ("Theory of a Method by which a Therapeutic Effective Dose can be Delivered into the Deeper Tissues without Injury to the Patient, at the Same Time Furnishing a Method of Protection against Radiodermatitis Superficially").

My second publication followed in the same year in "Münchener medicinischen Wochenschrift," 1909, No. 45, with the title "Zur Röntgentiefentherapie mit Massendosen" ("Concerning Deep Roentgen Therapy with Massive Doses").

My third publication may be found in "Strahlentherapie," Band 1 (1912), page 12, with the title "Röntgentiefentherapie mit Metallnetzschutz. Praktische Erfolge" ("Deep Roentgen Therapy with Wire Netting").

At that time the title of my publication was similar to the title of the article by F. Liberson, and, it may be observed, dealt with a similar method, at least, with the same principle though with modified details. The principle of Liberson's method and mine is also briefly as follows: If one wishes to deliver three to five erythema doses into a deep-lying tumor, one is apt to produce an injury to the skin which is difficult or impossible to heal. If, however, one utilizes a metallic mesh, or multi-perforated lead screen on the skin during the treatment, one may obtain in the perforations of the screen severe injury or burning, but under the metal wire or protected lines, the skin will remain practically uninjured, and from these lines, or small protected areas, healing of the injured skin can take place. By this means, the irradiation of the tumor area is not thereby interrupted, but homogeneously irradiated if one irradiates on each occasion with the focus of the tube shifted a millimeter or a centimeter in four different directions. Furthermore, in connection therewith, I have recommended tubes with broad focus, and I have also stated that herewith filters may be combined.

The fact that the same recommendations which I made in 1909 have also been made in December, 1932, indicates that the method has a future.

ALBAN KÖHLER

Wiesbaden, Germany

REPLY

To the Editor: Thank you for your kind letter of October 24, and the translation of Dr. Köhler's communication. I regret the delay in answering, but before the receipt of your letter, I was entirely unaware of Dr. Köhler's work on this subject, and had to get Dr. Köhler's publications translated for me before answering you. Now, after reading these translations of the articles, which he originally published in German in 1909 and 1912, I must admit that he described at that time the same general principle with the same goal in mind. Of course, he seems a bit uncertain as to the exact dosage he could deliver safely through his wire-gauze net; and he made no study of back-scattering, which, we know, limits the safe dosage by this method to four erythema units if the skin is to be left uninjured, instead of the 10 to 50 that he proposes. Furthermore, the bases for his method were expounded theoretically rather than proven experimentally. Probably all this depends upon the fact that the three years Dr. Köhler reported on the use of the wire screen were during the infancy of radiation therapy, when little was known of it; while the present author who, working independently, set out to study the theoretical, biological, and clinical phases of this principle, had the advantage of about twenty years of progress in this science.

It may be of interest to state here just how I first came to think of radiating numerous small areas through a perforator. About 1926 I was very much interested in the treatment of verrucæ vulgaris. As is well known to every roentgenologist, the dose necessary to cause a retrogression of the growth is usually from three to six erythema units. In one case there were a great number of plantar warts, and, instead of treating each individual area, which would have taken more than one hour, a piece of celluloid was placed over the plantar surface of the foot, and each wart was marked out on the celluloid. The celluloid was then transferred to a piece of lead 1 mm. in thickness, and we cut out with a knife openings slightly larger than those shown on the celluloid. The lead was then replaced on the skin and four erythema doses were given. About three weeks later it was noticed that wherever the lead partition was over 5 mm. long, and less than 1 mm. in thickness, the blister which formed was continuous, even on the part where that thickness of lead protected it from direct radiation. But in the areas that were small, less than 3 mm., and even though the adjoining circles or ovals met, the blister was not carried across from one area to the other. This led to the thought that if we could find the proper relation of the width of the lead to the perforated areas, we might have a method of administering larger doses of x-rays to deep-seated lesions.

The next step in this conception was rather a protracted one—finding a method to study the back-scattering of the protected parts of the perforator over a phantom which would simulate as nearly as possible the actual back-scattering on the skin at various radiation voltages, using the perforator. By July, 1931, I already had enough experimental data on this special way of studying back-scattering to permit the clinical trial of the method. I gave four erythema doses to the first patient, through the perforator, with such encouraging results that I was prompted to make a systematic study of the physical, biological, and clinical effects of various perforators and their reciprocals. These results were reported in November, 1932, at the meeting of the Radiological Society of North America.

In conclusion, I should like to say that there seems to be little doubt that Dr. Köhler thought of the principle before I even began medical school, and should be given all the rights that come with this priority. This does not in the least lessen my acute and continued interest in the method. I should like very much to see it given an extensive trial here, and will gladly continue to furnish perforators and reciprocals to any roentgenologist who desires to make use of this method in selected cases of deep-seated malignancies.

With kindest regard to Dr. Köhler and in the sincere hope that, with the added prestige his name gives the method, it will be applied more widely, I am

Sincerely,
F. LIBERSON, M.D.

THE FIRST DEEP RADIUM THERAPY

By WILLIAM ALLEN PUSEY, M.D., *Chicago*

My attention has recently been called to the fact that in "The Science of Radiology," authorized by the American Congress of Radiology, Dr. U. V. Portmann, in the

article on Roentgen Therapy, page 218, says upon the subject of early researches and biological effects that

"Nicholas Senn (114), of Chicago, really founded deep roentgen therapy when he reported favorable results from roentgen irradiation of the spleen in patients suffering from leukemia. This latter report proved that roentgen rays had deep effects because they reduced the size of the spleen and diminished the number of blood cells in the circulation. Senn, who was a well-known surgeon, had referred a patient with leukemia for treatment to Allen Pusey, a dermatologist and roentgen pioneer, who subsequently reported on the treatment of similar cases."

This (114) is a reference to a report by Dr. Senn, Medical Record, 1903, XLIV, 281.

This is an historical fiction that has been passing for a fact now for thirty years, since Dr. Senn made his report. But the actual facts are these:

Previous to the time of Senn's report the following reports of cases of leukemia and pseudoleukemia, treated with roentgen rays, in some cases with symptomatic cure, had been made:

Pusey, Jour. Am. Med. Assn., Jan. 18, 1902.
Pusey, Jour. Am. Med. Assn., April 12, 1902.
Hett, Dominion Med. Monthly, August, 1902.
Dunn, Am. Practitioner and News, October, 1902.
Childs, Med. News, January, 1903.
Williams, in his book on "Roentgen Rays," published about March, 1903.

Senn's only reports were April 18 and Aug. 22, 1903. Thus Senn's reports were more than a year after I had made the first reports of the use of x-rays in the treatment of leukemia and pseudoleukemia, and only after there were at least four reports by others in the literature on the subject. As a matter of fact, after my communication on this subject in the "Journal of the American Medical Association," Jan. 18 and April 12, 1902, and my demonstration of the cases before the Chicago Medical Society, Feb. 26, 1902, this method had become common knowledge and had been widely tried for a year before Senn made his report.

I had nothing to do with the x-ray treatment of Senn's cases, nor, I think, did Senn. I have always understood, but I do not know, that the suggestion to try x-rays in these cases was offered by one of the house staff of the Presbyterian Hospital, who was already familiar with the work that had been done with x-rays in these cases, and that it was carried out in Senn's cases by one of the staff of the hospital.

The Sociedad Argentina de Electro-Radiología Médica, of Buenos Aires, Argentina, announces the following officers: Sr. Presidente, Sr. Dr. José Guardado; Sr. Vice-presidente, Sr. Dr. M. Miranda Gallino; Sr. Secretario, Sr. Dr. Pedro A. Maissa; Sr. Tescrero, Sr. Dr. Cornelio Donovan; Sr. Vocal, Sr. Dr. Eduardo Lanari; Sr. Vocal, Sr. Dr. José A. Saralegui; Sr. Director de Publicaciones, Sr. Dr. José L. Molinari.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS

The sixth meeting of Michigan Association of Roentgenologists was held at Kalamazoo, Nov. 25, 1933. The program consisted of a symposium on Spinal Pathology, with the following speakers taking part:

F. C. Kidner, M.D., Detroit, Backache of Extrinsic Spinal Origin.
Harold Morris, M.D., Detroit, Urologic Disease as a Factor in Backache.
H. P. Doub, M.D., Detroit, Spinal Anomalies Mistaken for Fracture.
Carl Badgley, M.D., Ann Arbor, The Lumbosacral Joint.
E. R. Witwer, M.D., Detroit, The Differential Diagnosis of Deformities of the Vertebral Body.
E. W. Hall, M.D., Detroit, Prognosis of Vertebral Body Fracture.

The following officers for the coming year were elected: M. W. Clift, M.D., of Flint, *President;* F. J. Hodges, M.D., of Ann Arbor, *Vice-president,* and S. W. Donaldson, M.D., of Ann Arbor, *Secretary-Treasurer.*

A REQUEST

I will be grateful for the assistance of any one who has observed the effects produced by the presence of misplaced buried teeth (aberrant teeth) and impacted teeth, who will help me gather material for an article on this subject to be written in collaboration with L. Monier, M.D., D.S., Paris.

I will appreciate any information sent to me bearing upon the following points, as well as for

any reprints, clippings, or references to articles or books touching on the same:

A. At what age and how was the tooth (or teeth) discovered?

B. At what age was the tooth (or teeth) removed?

C. Has malignancy been observed to precede or follow the removal of such tooth (or teeth) or failure to remove the same?

D. What signs, symptoms, or effects—local, general, or special—drew attention to such a tooth (or teeth) or accompanied the presence of the same?

E. What method was employed to remove the same?

F. What anesthetic was used?

G. What effect, if any, did the removal have upon the previously mentioned signs, symptoms, or effects?

H. Did the removal of the tooth (or teeth) have any effects other than those previously mentioned? Complications?

I. The sex of the patient.

J. The race of the patient.

K. The *position* of the tooth (or teeth). Any prints of x-ray plates or films, or tracings of same, or diagrams or drawings showing the position and relation to other teeth or other structures will be valuable and appreciated. These will be returned, if requested, and credit will be given for any material used. Please write name and address plainly.

Yours sincerely,

ALONZO MILTON NODINE,
D.D.S. (N. Y. Univ.), L.D.S.R.C.S. (Eng.),
L.R.C.P. (Lond.), M.R.C.S. (Eng.)
117, The Ridgway,
Wimbledon,
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England.

CORRECTION

The authors of the paper entitled "Progress in the Design and Manufacture of X-ray Tubes," in RADIOLOGY for October, 1933, page 372, desire to make a correction in their Table II. It is correct as printed below.

TABLE II.—COMPARISON OF FOCAL SPOT DESIGNS WITH RESPECT TO INFLUENCE ON RADIOGRAPHIC FACTORS

All factors expressed in arbitrary units unless otherwise stated

Focal Spot Design		Distance (of Focal Spot to Part Radiographed)	Detail (for a Given Part—Film Distance)	Radiog. Speed (*b*)	Maximum Allowable Film Dimension (*c*)	Power Required
Area of Impact (*a*)	Angle (with Respect to a Line Normal to Film)					
a	ϕ	d	$D = \frac{.84d}{\sqrt{a \sin \phi}}$	$s = \frac{a}{d^2}$	$L = d \tan \phi$	$p = a$
1.0	45°	1.0	1.0	1.0	1.0	1.0
4.0	45°	1.0	0.50 (poorer)	4.0 (faster)	1.0	4.0
4.0	45°	2.0	1.0	1.0	2.0	4.0
1.0	20°	1.0	1.4 (better)	1.0	0.36	1.0
2.1	20°	1.0	1.0	2.1	0.36	2.1
7.6	20°	2.75	1.4	1.0	1.0	7.6
1.0	10°	1.0	2.0 (better)	1.0	0.18	1.0
4.0	10°	1.0	1.0	4.0	0.18	4.0
33.0	10°	5.7	2.0	1.0	1.00	33.0
1.0	90°	1.0	0.84 (poorer)	1.0	large	1.0
0.71	90°	1.0	1.0	0.71 (slower)	large	0.71

(*a*) In all cases it is assumed that the shape of the area of impact is such that its projection on the film is a circle.

(*b*) It is assumed that radiographic speed is a function of area of impact and tube-part distance. This is true only for short exposures in which area of impact rather than heat conduction from the focal spot is the controlling factor in determining the maximum allowable tube power.

(*c*) This comparison holds assuming either that the film size is limited by difference in detail over the film or by the actual size of the useful beam of x-rays.

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APPARATUS

Photographic Considerations about the Comparison between Roentgenograms on Film and on Paper. Richard Herz. Röntgenpraxis, April, 1933, V, 260–266.

Comparisons between roentgenograms on film and on paper are not easy matters. The author has experimented from a purely photographic standpoint and shows that roentgen paper cannot take the place of the double coated film under most conditions. Photometric registration of differences in blackening indicates that the amplitude in films is much wider; that is, there is much better contrast on films. The theoretic considerations and the experimental work done by the author will be of interest to roentgenologists who are interested in the use of paper films.

H. W. HEFKE, M.D.

Comments on the Higher X-ray Voltages. Albert Soiland. Jour. Am. Med. Assn., Sept. 30, 1933, CI, 1055–1057.

There are only two institutions which have successfully maintained a therapeutic voltage over 500,000 for an appreciable time period in the United States. From a survey of the results of efforts in developing the higher x-ray voltages up to the present, one may accept as a fact that the shortest effective wave length now available corresponds to a voltage of between 500,000 and 600,000. At these potentials, a tube carrying 5 milliamperes emits a radiation intensity that is comparable to that from approximately 500 gm. of radium. From an economic standpoint, therefore, the comparison is very largely in favor of the x-rays. With approximately 500 kilovolts on the tube, practically a 45 per cent depth dose is obtained with the Lauritsen tube at the level of 10 cm. from the surface, thus opening up a field to high voltage roentgen therapy not hitherto obtained. It is possible, when its distribution has become more generalized, that it may supplant the use of the large and expensive radium pack or radium gun, affording the opportunity to convert the latter into highly filtered platinum needles or tube applicators for interstitial use. In the near future radium will be employed largely for interstitial applications, and short wave x-rays for treatment from the exterior.

To Dr. Lauritsen belongs the credit of being first in the field with a practical high voltage x-ray tube, one of which, to his knowledge, has functioned satisfactorily under a voltage of 1,200,000. It is this type of tube, an early edition of which has been in operation for over two years, with no serious breakdown, that has a record of a total number of x-ray hours unheard of in any tube that has ever been presented for therapeutic work.

C. G. SUTHERLAND, M.D.

BACTERICIDAL EFFECTS

The Correlations between Changes in the Ability of the Reticulo-endothelial System to Absorb Dyes, the Bactericidal Power of the Blood, and the Mineral Metabolism of the Tissue in Irradiated Rabbits. Y. Koga. Strahlentherapie, 1933, XLVII, 201–232.

From his experiments the author concludes that the ability of the reticulo-endothelial system to absorb dyes is increased by small doses of roentgen rays (42 r). The effect is noticeable one hour after the exposure. After larger doses (120 r) are used this effect manifests itself after three hours. He believes that this is another proof for the Arndt-Schultz law. The bactericidal power of the blood shows periodical fluctuations after irradiation of the rabbit. For these observed phenomena the mineral metabolism and perhaps the ion concentration of the cells is of great importance. The sum total of the calcium and potassium in the liver and spleen corresponds to the changes in the amount of dye deposited in these organs.

ERNST A. POHLE, M.D., Ph.D.

BONE DISEASES (DIAGNOSIS)

Osteopetrosis: Report of Case. O. B. Mayer and T. A. Pitts. Jour. Am. Med. Assn., July 1, 1933, CI, 22–24.

Osteopetrosis is commonly spoken of as "marble bone"; recently it was referred to as "chalky bones." The condition was first described by Albers-Schönberg in 1904. A total of 48 cases has been reported in the literature. The outstanding characteristic is generalized increased radiopacity of all bones due to the high calcium content.

A spontaneous fracture of the femur in a girl, aged 11, was roentgenographed and the film showed the condition. The girl was born after the mother had experienced three uninduced miscarriages and a stillbirth. The mother's first two pregnancies produced normal children. During the latter months of gestation the mother subsisted largely on sweet milk. Because of suspected blindness the child was not permitted outdoors until early childhood and had little exposure to the sun's rays. No cod-liver oil had been given at any time. In 1932, at the age of 17, she showed a marked secondary anemia.

C. G. SUTHERLAND, M.D.

BONE DISEASES (THERAPY)

Roentgen Therapy of Polycythemia Rubra. H. Holfelder and A. Reisner. Strahlentherapie, 1933, XLVII, 274–290.

In polycythemia rubra irradiation of the bone marrow through large areas with high doses of heavily filtered roentgen rays is the method of choice. The authors relate their experience in the treatment of 15 cases. They first administered from 30 to 50 per cent

H.E.D. in from 6 to 8 single sittings at intervals of from 5 to 8 days. They found, however, that this dose was not effective, so they increased the single doses to from 70 to 90 per cent H.E.D. The total dose given amounted then to from 6,000 to 12,000 r in from 4 to 7 weeks. Sternum, scapula, pelvis, and spine were exposed.

ERNST A. POHLE, M.D., Ph.D.

CALCULI

Ureteral Calculi. George R. Livermore. Am. Jour. Surg., May, 1933, XX, 214–222.

The author gives a brief résumé of the etiology, symptoms, and treatment of ureteral calculi. He believes that infection, stasis, and faulty metabolism are the chief factors in the etiology of urinary calculi.

The symptoms of ureteral calculi vary according to the character of the obstruction, the degree of infection, and the condition of the kidneys. Eisendrath and Rolnick enumerate six different clinical types: (1) those with predominant symptoms of renal infection, with or without a history of pain or colic; (2) those in which pain is the outstanding feature; (3) those in which anuria is predominant; (4) those presenting evidence of non-infected hydronephrosis; (5) those in which a hematuria or pyuria without localizing signs is present; (6) those presenting no symptoms and latent cases.

The differential diagnosis from disease of the gall bladder, appendix, colon, and female pelvic organs is at times not easy, and it is here that cystoscopy and the x-ray prove so invaluable. The methods distinguishing ureteral shadows and their interpretation are mentioned.

Treatment of ureteral calculi depends upon (1) the size, (2) the number, (3) the location, (4) the condition of the patient, and (5) the functional capacity of the kidneys. A discussion of these factors is included in the article.

Dr. Livermore has devised an ingenious instrument for dislodging and eliminating calculi of the ureter.

DAVIS H. PARDOLL, M.D.

CANCER (DIAGNOSIS)

Tubelike Infiltrative Mucinous Carcinoma of the Rectum in a 19-year-old Patient. Charles S. Higley. Jour. Am. Med. Assn., Aug. 12, 1933, CI, 523, 524.

This case is reported because of the unusual type of the tumor, which converted the rectum into a rigid, firm tube as disclosed by clinical and pathologic examination. A survey of the literature elicited one direct reference to this form of tumor and three similar cases, without information as to age, sex, or special microscopic features. The lesions extended 7, 18, and 20 centimeters, respectively, in the rectosigmoid region.

The patient was a male, aged 19, who recalled that six months before admission his stools were occasionally blood-streaked. Four months previously there had been a decrease in the caliber of the stool and some pain on defecation. Two weeks before admission, after taking some highly seasoned food, the patient developed severe abdominal cramps, followed by diarrhea, and pain in the left lower quadrant. Proctoscopic examination showed a uniform narrowing of the lumen, while biopsy revealed mucinous carcinoma. After an exploratory laparotomy and colostomy, the patient died on the sixth day from pulmonary embolism. Necropsy showed a well-differentiated mucinous adenocarcinoma, with areas of anaplasia.

C. G. SUTHERLAND, M.D.

The Early Diagnosis of Malignant Disease. Current Comment, Jour. Am. Med. Assn., July 8, 1933, CI, 129.

A roentgen examination may give valuable aid, especially when there is a suspicion of cancer of the alimentary canal. The roentgenograms should be made and interpreted by an expert radiologist after a conference with the clinician. This method applies also to the investigation of suspected tumors of bone and other tissues. Definite diagnosis frequently demands the services of a diagnostic "team," including a clinician, a radiologist, and a surgeon. Too much reliance, however, is sometimes placed on the histologic appearance of tissue removed at biopsy, and sometimes on the roentgen examination alone—roentgen examination will reveal cancer of the stomach in the early stages in nearly every case. The precision of such an examination has increased so rapidly that even many physicians are not aware of the exactitude with which diagnosis can be reached.

C. G. SUTHERLAND, M.D.

Carcinoma of the Stomach in the First Two Decades of Life. M. K. King. Jour. Am. Med. Assn., Aug. 12, 1933, CI, 520–522.

Carcinoma of the stomach is rare in patients under 30 years of age. Before the age of 20 it is so rare that those cases which have occurred have usually been the subject of individual reports. The author collected 40 cases of cancer of the stomach occurring in the first two decades of life, the youngest an infant whose symptoms began on the tenth day of life and death occurred in the fifth week. Death in the majority occurred in from a few weeks to a few months, the mortality in the younger patients being 100 per cent.

He reports a case of a negro youth, aged 20 years, with a three-weeks history of a severe burning pain in the upper part of the abdomen, accompanied by

nausea and vomiting, intermittent at first and later becoming almost continuous. There was a 15-pound weight loss in one month. He was operated on two and a half weeks after admission, the lesion being found inoperable. A gland was taken from the mesentery, microscopically examined and diagnosed carcinoma. The patient died three months after the onset of symptoms, or nine weeks after admission to the hospital.

C. G. SUTHERLAND, M.D.

CANCER (THERAPY)

Radiation Therapy of Carcinoma of the Penis. Wilhelm Schloss and Franz Urbach. Strahlentherapie, 1933, XLVII, 443.

The authors report their experience in the treatment of 10 cases with carcinoma of the penis: 6 of these were free of symptoms at the time of report, 2 of those longer than 1 year, one case 6 months, 1 case 3 months, and 2 cases 6 weeks. Another case was improved, while two did not respond and one far advanced case died shortly after the treatment. The radium technic is described in detail. It is essential that a sufficient dose be given, with homogeneous distribution.

ERNST A. POHLE, M.D., Ph.D.

The Surgical and Radiotherapeutic Treatment of Carcinoma. Hans R. Schinz. Strahlentherapie, 1933, XLVII, 453.

The author outlines in detail the indications and contra-indications for radiation therapy in carcinoma, particularly of the cervix and of the skin. Statistical methods are analyzed and some of the common errors mentioned. The limitations of electrocoagulation in the treatment of skin carcinoma are emphasized. The article is recommended for study in the original.

ERNST A. POHLE, M.D., Ph.D.

The Rôle of the Radiologist in the Treatment of Cancer. George W. Grier. Jour. Am. Med. Assn., Sept. 23, 1933, C1, 965, 966.

The therapeutic effect of x-rays was an early observation, and the technic was promptly and efficiently developed. With the advent of the Coolidge tube the x-ray treatment of malignant conditions of the skin was accepted as a superior method and, with the advantages of accurate dosage and unlimited quantities of radiation which became available with the Coolidge tube and improved apparatus, all other methods of treatment have been practically abandoned. The scope of the method was broadened by the introduction of radium as a therapeutic agent, when lesions in the cavities of the body were added to the list of those which could be successfully treated.

It is the duty of every radiologist to keep abreast of the progress of his specialty. He has a responsibility in the cancer problem which he cannot evade and a moral obligation to the people in his community to provide them with whatever benefits may be obtained from radiation therapy.

C. G. SUTHERLAND, M.D.

Carcinoma of the Cervix Not Cured by Radiation. Friedrich Voltz. Strahlentherapie, 1933, XLVII, 475.

The author studied 352 cases of carcinoma of the cervix which were treated by irradiation during the period 1921–1927 in the Women's Clinic, University of Munich. Group 1 comprises operable cases and Group 2, borderline cases. An analysis of the 50.6 per cent cases in Group 1 and the 73 per cent of the cases in Group 2 who died before the five-year period had elapsed, permitted certain conclusions as to the failure of radiation therapy. (1) The age of the patient is of definite influence on the final result. (2) It is essential to start treatment as soon as possible after the first symptoms appear. (3) The social status of the patient is also of influence. (4) The importance cannot be over-emphasized that a minimum dose, at least, must be applied. (5) There is also a probability that the histology of the tumor has certain relations to the final result and that some hereditary factors play a rôle in the final outcome.

ERNST A. POHLE, M.D., Ph.D.

The Curability of Cancer of the Colon, Rectosigmoid, and Rectum. Fred W. Rankin. Jour. Am. Med. Assn., Aug. 12, 1933, CI, 491–495.

The youth of an individual is an unfavorable factor as compared with the less active tissue barriers of middle life or advancing years. The duration of the growth is a factor of importance. The size of the growth has little if anything to do with the prognosis—growths on the right half are usually large, ulcerating, and infected, whereas those in the sigmoid are the smallest, yet the left colonic lesions are somewhat poorer of prognosis than are tumors on the right half. The direction of growth is of considerable importance. Whenever cancer of the large bowel, rectosigmoid, or rectum takes on the appearance of a polypoid or adenoid-like growth and pouches into the lumen of the bowel, one finds a malignant condition of low or average grade and little or no nodal involvement. When the growth is a punched-out ulcer with a large active base penetrating toward the serosal coat of the bowel, one is more likely to find a higher grade of malignancy and a larger percentage of nodal involvement.

C. G. SUTHERLAND, M.D.

CONTRAST MEDIA

Hepatosplenography with Thorium Dioxide Sol: Clinical Experience with 100 Patients. Wallace M. Yater and Laurence S. Otell. Jour. Am. Med. Assn., Aug. 12, 1933, CI, 507–514.

The authors had used this metal for roentgenographic demonstration of structural changes in the liver and spleen for nearly two years, in a large series of patients, without having noted any serious immediate or remote effects. Since the unfavorable report of the Council on Pharmacy and Chemistry of the American Medical Association they have confined the use of the metal to patients who do not have a reasonable chance of long life.

The method has proved of value: (1) To detect the nature of a mass in the upper part of the abdomen; (2) to determine the presence and kind of hepatic disease (atrophic cirrhosis, hypertrophic cirrhosis, syphilis of the liver, metastatic malignant lesions, primary tumor, abscess, cyst, and amyloidosis); (3) to ascertain whether or not metastatic lesions are present in the liver if operation is contemplated for cancer; (4) to determine rupture of the liver or spleen; (5) to determine the cause of jaundice (whether intrahepatic or due to obstruction of the common bile duct); (6) to follow the progress of hepatic or splenic disease; (7) to demonstrate whether a lesion is above or below the diaphragm; (8) to diagnose ascites; (9) to study diseases of the spleen.

The method of administration and the reactions are discussed in detail.

C. G. SUTHERLAND, M.D.

CYSTS

Congenital Air Cyst of the Lung: Report of Case. C. V. Croswell and J. Cash King. Jour. Am. Med. Assn., Sept. 9, 1933, CI, 832–834.

Few large solitary air cysts or "balloon cysts" of the lung have been reported in the American literature. Of 108 cases tabulated by Koontz in 1925, only seven were of the solitary type. Twelve additional cases have been reported in the American literature since that year. These cysts are unilateral and develop in the left lung far more frequently than in the right. The authors report a case in a boy aged 3 whose roentgenograms showed complete absence of normal lung tissue on the left side. The left side of the diaphragm was displaced downward and there appeared to be a herniation of the air sac through the anterior superior mediastinum. Bronchoscopic examination showed the left main bronchus to be stenosed by apparently extraneous pressure. Four thousand c.c. of air was aspirated, aspiration being necessary every four to six hours. Iodized oil was injected and improvement was noted within seven days. In time, the cystic air sac had almost completely collapsed, and the child's progress has been satisfactory to date.

Most theories postulate an embryonic defect in the development of the bronchus. Histologic studies reveal that the walls of a cyst have the characteristics of a bronchiole. The developmental error may interfere with the normal growth of the alveolar tissue, leaving the bronchi unsupported and thus permitting undue dilatation. S. Smith (Congenital Cystic Diseases of the Lung, British Med. Jour., May 30, 1925, I, 1005) thought sacs were formed in fetal life before the time for development of the alveolar tissues. A small congenital bronchiectatic cavity gradually grows as the infant breathes. At the bronchial opening is a one-way valve mechanism which allows air to enter the sac and inflate it, but does not allow a corresponding deflation to take place. As the cavity grows in size the bronchial radicle or radicles leading to it become more and more tortuous as they are compressed toward the hilus, thus increasing the interference with deflation.

The cysts, during fetal life and a variable period of natal life, contain fluid and do not have a patent bronchial connection. At a certain stage they rupture into one or more bronchi, whereupon the fluid contents are coughed up and replaced by air.

C. G. SUTHERLAND, M.D.

DIAPHRAGMATIC HERNIA

Case Report of a Right-sided Diaphragmatic Hernia. Kurt Breckoff. Röntgenpraxis, April, 1933, V, 257, 258.

Non-traumatic right-sided diaphragmatic hernias are apparently rare, since the author could find only two such cases in the German literature. The case cited was that of a 59-year-old woman who came for roentgenologic examination of the gastro-intestinal tract because of symptoms seeming to indicate a carcinoma. Such was demonstrated roentgenologically in the pyloric portion. On a film taken 8 hours after the barium meal, a barium-filled loop of intestine was seen above the diaphragm in the right cardio-phrenic angle. A barium enema showed a herniation of part of the transverse colon through the diaphragm. At operation, the carcinoma was removed and a herniation of the transverse colon through the foramen venæ cavæ, which admitted three fingers, was seen. The bowel was freed from adhesions, replaced in the abdominal cavity, and the opening in the diaphragm sutured. Two months after operation the patient had no symptoms referable to the gastro-intestinal tract.

H. W. HEFKE, M.D.

Diaphragmatic Hernia: Symptoms and Surgical Treatment in 60 Cases. Stuart W. Harrington. Jour. Am. Med. Assn., Sept. 23, 1933, CI, 987–993.

Special roentgenologic examination in recent years has greatly increased the number of cases recognized, most of this increase being represented by the paraesophageal type of hernia. A large percentage of these

hernias affect old people with mild symptoms; in others, more serious disease contra-indicated surgery. Some of the unsatisfactory results from operative procedures, particularly those on the gall bladder, stomach, and appendix, are due to unrecognized diaphragmatic hernias. Examination of the diaphragm in the course of abdominal operations occasionally reveals a hernia that has not been recognized clinically or roentgenologically. The condition is apparently more common than the present records would indicate.

Non-traumatic diaphragmatic hernias may be congenital or acquired. Traumatic diaphragmatic hernia may be caused by an indirect or by a direct injury to the diaphragm. Operative replacement of the herniated viscera in the abdomen, with repair of the abnormal opening in the diaphragm, is the only treatment that insures complete relief.

C. G. SUTHERLAND, M.D.

FOREIGN BODIES

Four Hundred Ninety-seven Foreign Bodies in the Stomach. London letter. Jour. Am. Med. Assn., July 8, 1933, CI, 151.

The practice of some lunatics of swallowing all sort of articles is well known, but the discovery of 497 articles, weighing three and one-half pounds, in a man's stomach constitutes a record.

A farmer, aged 28, died in the County Mental Hospital following an operation. In his stomach were found 200 nails from one-half to four and one-half inches long, 36 staples, 43 phonograph needles, 6 teaspoons, 3 table forks, 7 coins, 6 brace buckles, 3 door keys, 3 penknives, 3 S-shaped meat hooks, 10 safety pins, 4 sewing needles, 6 pins of ordinary type, 13 pieces of glass or earthenware, and 9 screws. The medical superintendent stated the man had a delusion that his stomach was too smooth. Death was due to ulceration of the stomach, and hemorrhage.

C. G. SUTHERLAND, M.D.

GALL BLADDER (NORMAL AND PATHOLOGIC)

Cholecystitis: Study Based on Follow-up after from 5 to 15 Years of 200 Patients Not Operated on. J. M. Blackford, Robert L. King, and K. K. Sherwood. Jour. Am. Med. Assn., Sept. 16, 1933, CI, 910–913.

Disease of the gall bladder is diagnosed in the authors' clinic more often than any other chronic intra-abdominal lesion. Twelve years ago they reported that gall-bladder disease was found twice as frequently as peptic ulcer and gastric cancer combined, and that it was the most common organic cause of dyspepsia. Six per cent of all their patients over 20 years ago were diagnosed as having gall-bladder disease, yet pathologic studies indicate that ten times this percentage, or 60 per cent, of adults, show cholecytopathies at routine autopsies. Thirty-seven per cent of chronic cholecystitis patients have had satisfactory relief over an average of more than eight years without operation. Forty-eight per cent of patients with chronic cholecystitis who were not operated on have either had or should have had surgical intervention on account of continuation of symptoms. Fifteen per cent of patients are dead, but only 1 per cent died directly from gall-bladder disease. The patient with uncomplicated cholecystitis should be given a trial on medical treatment; if not markedly relieved promptly, he should be operated on.

C. G. SUTHERLAND, M.D.

GASTRO-INTESTINAL TRACT (DIAGNOSIS)

Submucous Lipoma of the Cecum. H. R. DeLuca and Philip Henstell. Jour. Am. Med. Assn., July 22, 1933, CI, 277, 278.

Of the 181 cases of lipoma of the gastro-intestinal tract reported by Comfort in 1931, only 16 were in the cecum alone: of these, 12 were with symptoms and four were without. The two conditions most usually confused with cecal lipoma are appendicitis and carcinoma—the authors present one case giving features simulating both. The diagnosis is rarely, if ever, made before operation.

Roentgen examination of the colon by a barium enema revealed no obstruction to the passage of the barium until it reached the first portion of the transverse colon, where it stopped at a dilatation of the bowel. After one hour a small amount entered the hepatic flexure, where there appeared to be marked infiltration of the wall and canalization with dilatation of the transverse colon. The opinion of the roentgenologist was that there existed a malignant growth which caused an obstruction. Operation nine days after admission revealed a large mass in the wall near the ileocecal valve. Carcinoma of the cecum and ascending colon was suspected and resection was done. The pathologic diagnosis was submucous lipoma of the cecum.

C. G. SUTHERLAND, M.D.

GASTRO-INTESTINAL TRACT (THERAPY)

Care of Advanced Carcinoma of the Gastro-intestinal Tract. Frank C. Yeomans. Jour. Am. Med. Assn., Oct. 7, 1933, CI, 1141–1145.

This report is on patients admitted to the New York City Cancer Institute, a municipal institution into which no patient is denied admission. Consequently, a large field for palliation is available. The incidence of gastro-intestinal malignant conditions included esophagus 192; stomach 622; colon 77; sigmoid 70; rectum 406; anus 17. Gastro-intestinal tract cancers constituted 1,384 (13.7 per cent) of all admissions.

Nourishing food of high caloric value is essential, also good hygiene and competent nursing, together with rest and sufficient sleep—obtained, as necessary, by sedatives, analgesics, or opiates.

In carcinoma of the esophagus, gastrostomy should be performed as soon as solids will not pass the stenosed lumen and nutrition begins to fail. This procedure is also followed in some cases of carcinoma of the cardia.

In carcinoma of the stomach with obstruction, gastroenterostomy, with implant of gold seeds of radon into the malignant area, gives a high degree of palliation.

Different forms of short circuiting, as indicated, are used in carcinoma of the colon. Colostomy and radical surgery give best results in carcinoma of the sigmoid. In carcinoma of the rectum, colostomy is beneficial and affords an avenue for effective irrigation. A colostomy under dietary control is much less objectionable than is popularly believed. The wearing of a receptacle should be avoided, if possible. A cycle of high voltage roentgen therapy is frequently successful in checking rectal hemorrhage, sometimes even retarding the progress of the disease. When accessible, the tumor is treated most satisfactorily by interstitial seed implants inserted directly by trocar. After the reaction from the irradiation has subsided, the tumor in many instances shrinks noticeably or is held in abeyance; the discharge is reduced, the pain is relieved, all for varying periods.

The preferable treatment for epithelioma of the anus is irradiation by intratumoral seed implants of radon. The palliation resulting from electrosurgery is well worth the effort. Subarachnoid injections of absolute alcohol for relief of peripheral pain has been employed with gratifying results in seven cases.

C. G. SUTHERLAND, M.D.

GYNECOLOGY AND OBSTETRICS

The Importance of Roentgen Rays for Gynecological Diagnosis and Investigation. Rudolf Dyroff. Röntgenpraxis, April, 1933, V, 241–248.

This is an historical review of the roentgenologic methods employed in gynecology and obstetrics. The value of these methods for modern gynecology is evaluated and the indications for special procedures (pneumoperitoneum, hysterosalpingography, the combination of both, etc.) are given. The author has investigated two new methods, which are as yet in the experimental stage, but may in the future be of some diagnostic value. The first is the filling by thorotrast of the blood vessels of the female genital organs, which are shown on roentgenograms, if films are taken during or directly after the injection. It may help in the differentiation of early pregnancy, tubal pregnancy, for demonstration of the seat of the placenta (placenta prævia), and for the showing of sites of tumors. As yet the injection is difficult, but the author hopes to perfect it. Another method is the infiltration of the pelvic tissues with thorotrast, the attempts being primarily of a therapeutic nature. It was shown that carcinomatous metastases, for instance, showed filling defects and could be differentiated from a normal or inflammatory parametrium. If the contrast material was injected into the tumor tissue itself, it remained in the tumor tissue only. The author is of the opinion that this method, after it has been perfected, will be of great help for the diagnosis of parametritis and carcinomatous metastases.

Hysterography by injection of contrast material into the uterus is not a method of diagnosing early pregnancy, because there is always the danger of abortion. A flat film of the abdomen allows in most cases a diagnosis of pregnancy after the third or fourth month. Death of the fetus may sometimes be diagnosed in roentgenograms by an atypical curve of the spine and displacement of the bases of the skull. Twins and triplets can be diagnosed, also congenital anomalies of the skeleton. The position of the fetus and the relative size of its head may be shown, especially well on lateral stereograms. The roentgenologic diagnosis of type and degree of contracted pelvis is of great importance. Three methods are at present available for correct pelvic measurements (Martin's, Guthmann-Dyroff's, stereograms). Guthmann-Dyroff's method is a simple and inexpensive one, giving a correct measurement of the conjugata vera. However, for the correct understanding of size of pelvis and size and position of the fetal head, lateral stereograms are necessary, according to Dyroff. The roentgen ray has also contributed considerably to the knowledge of physiology of the female genital tract (peristalsis of tubes, changes in tone and motility by ovulation, etc.).

H. W. HEFKE, M.D.

Pneumonococcic Infection of the Sacro-iliac Joint Complicating Pregnancy: Treated by Radical Resection of the Ilium. Fremont A. Chandler. Jour. Am. Med. Assn., July 8, 1933, CI, 114–116.

Acute pyogenic infections of the sacro-iliac joints have long been recognized as severe menaces to life. The extension into the fascial planes of the pelvis and the development of an osteomyelitis of the ilium or sacrum is to be anticipated. In a review of the literature since 1860, no case of pneumococcus infection of the sacro-iliac joint was found, nor reference to such an infection complicating pregnancy.

The author reports two cases. The first, a woman, aged 20, complained of pain in the right leg of two days' duration following an abortion 16 days before. Lateral compression of the iliac crests caused excruciating pain in the region of the right sacro-iliac joint. Roentgenograms showed some thinning of the joint space and some lack of bone definition. An exploratory needle inserted into the inferior aspect elicited pus.

The second was a woman, aged 28, in the eighth

month of her second pregnancy. Lateral compression of the iliac crest caused severe pain in the left posterior buttock. Roentgenograms failed to reveal pathologic changes in the region of the sacro-iliac joint because of the overlying fetal head. Aspiration was negative in results. Eleven days later roentgenograms showed definite evidence of a destructive process involving the lower left sacro-iliac joint. Six days later an abscess overlying the sacrum and region of the ilium adjacent to the sciatic notch was drained and a block of ilium was removed.

C. G. SUTHERLAND, M.D.

HEART AND VASCULAR SYSTEM

The Radiology of Heart Disease. John Parkinson. British Med. Jour., Sept. 30, 1933, No. 3795, pp. 591–594.

In the modern diagnosis of cardiovascular disease, radiology has taken an important and essential place comparable with that of electrocardiography. The sphygmomanometer, the electrocardiograph, and x-rays represent the current demand for precision, for thereby many fallacies inherent in the personal factor are eliminated.

The heart is a rounded organ hanging in a rounded thorax, and the old scheme of it as a flat solid applied to the anterior chest wall is inconsistent with our modern conception of it as a three-dimensional structure. Percussion thus gives a rough idea of the transverse width of the heart in a single plane and that only under favorable conditions. Obesity and emphysema increase the difficulty of determining the size, shape, and position of the heart.

The heart is well placed for inspection by x-rays, surrounded as it is by translucent lung, and we have a vivid method of applying anatomy and morbid anatomy to the study of the heart in living patients. The author stresses the great importance of studying carefully and knowing thoroughly the many variations of the normal heart in all positions.

In the radiological examination of the heart, the routine anterior film alone is often inadequate. The author suggests radioscopy in the anterior and both oblique positions, to be followed by teleradiograms in the anterior and left oblique, with or without the right oblique. The visualization of the esophagus often helps in determining enlargement of the left auricle. The shape of the heart is considered of more importance than its size. It is more useful to decide whether the heart is misshapen by pathological change than whether it is enlarged as a whole.

The true value of radiological examination of the heart is realized in the study of mitral stenosis. It is now accepted that, after the characteristic murmur, particular enlargement of the left auricle, as seen in the right oblique position, is the surest sign of this disease.

In aortic incompetence, enlargement of the left ventricle is the conspicuous feature. If the aorta is sufficiently widened or aneurysmal, the syphilitic etiology of the lesion will be suggested.

Congenital malformations may be more frequently distinguished from rheumatic heart disease in young children. In most cases of goiter no cardiac enlargement may be present. In more advanced cases generalized enlargement of the cardiac shadow results. Other conditions which may be noted in the radiological examination while studying the heart are as follows: Pulmonary disease, intrathoracic tumors, intrathoracic goiter, and hydrothorax.

J. N. ANÉ, M.D.

Radiology in Heart Disease. Peter Kerley. British Med. Jour., Sept. 30, 1933, No. 3795, pp. 594–597.

The author considers simple screening as the most important method of x-ray examination of the heart. Orthodiagraphy, teleradiography, and kymography are additional methods. The oldest of these is orthodiagraphy, which employs only the central ray. Accurate measurements may be made on the tracings obtained. Teleradiography has many advantages over orthodiagraphy but is a more expensive method. Kymography, which is the most recent method, makes use of a fine slit, fixed over the border of the heart. The x-rays are projected through this slit, and a film is made on which is recorded a zigzag image representative of the pulsations of the heart.

The x-ray appearance of the normal heart varies with the age, sex, and habits of the patient. In the average adult the heart shadow is of the so-called oblique type, its transverse diameter bearing a relation to the chest width of 1 to 2. This ratio is known as the "heart-lung coefficient." The right border of the normal heart shadow is formed by the right auricle, which is separated from the shadow of the ascending aorta by a well-defined notch. The left border is formed partly by the edge of the left ventricle and partly by the edge of the appendage of the left auricle. The latter is separated by a notch from the shadow of the pulmonary artery. The popular idea that a notch separates the ventricular shadow from the auricular one is erroneous. The two shadows merge together imperceptibly and it is only when the heart is diseased that they appear as separate entities.

The situation of the diaphragms rather than the shape of the bony thorax appears to be the chief factor in the production of the so-called small heart. When for any reason the diaphragm is depressed the heart rotates slightly to the right and forward, and consequently appears smaller on the radiograph. The author has made some observations and has found that a woman, who normally has a small heart, has a transverse and apparently wide heart during the last two months of pregnancy. The alteration occurred with the elevation of the diaphragm, and about six

weeks after delivery the diaphragm was back in its normal position and the heart again appeared to be small. The author further believes that the small heart associated with chronic pulmonary tuberculosis is the result of rotation of the heart to the right, following the depression of the diaphragm by compensatory emphysema, and not the result of atrophy of the heart muscle.

A differential x-ray diagnosis of the cause of cardiac enlargement is not possible unless the enlargement is associated with some definite alteration in the shape of the heart or great vessels. The most characteristic alterations in the shape of the heart are produced by congenital and valvular disease. Nearly all congenital lesioes with an admixture of the venous and arterial streams show enlargement of the pulmonary artery, which appears as an additional bulge on the left border of the heart just below the aortic knob.

Coarctation of the aorta reveals itself radiographically by enlargement of the left ventricle, disappearance of the shadow of the aortic knob, and visible erosion of the lower borders of the ribs due to the dilatation of the intercostal arteries forming a collateral circulation. A left oblique view may reveal the actual stenosis.

Aortic regurgitation and mitral stenosis cause typical alterations in the shape of the heart shadow. In a well-established case of mitral stenosis the right border of the heart shadow is unaltered, and the left border shows a small aorta, a large pulmonary artery, and an extra bulge caused by enlargement of the appendage of the left auricle. The enlarged left auricle may result in displacement of the esophagus. The normal angulation at the bifurcation of the trachea may be increased, and result in hemoptysis from pressure.

Passive hyperemia of the lungs caused by mitral stenosis or heart failure gives remarkable and varied x-ray appearances. In the early stages there is noted a generalized loss of translucency and marked increase in the density of the vascular shadows. The hilar shadows are enlarged and the movements of the diaphragms are restricted. The loss of translucency is due to compression of the alveoli by the distended capillaries, and the enlarged hilar shadows and coarse vascular markings result from distention of the pulmonary vessels. If the hyperemia becomes chronic, the loss of translucency is more marked, and the vascular striæ in the lungs become still coarser and wider because the perivascular lymphatics now show up. Certain cases of chronic hyperemia give rise to a miliary appearance in the lungs. These miliary spots, which are scattered all over both lungs in chronic hyperemia, are caused partly by dilated capillaries seen end-on and partly by exudation of heart-failure cells into the alveoli. A severe attack of passive hypermeia always leaves permanent radiological evidence behind it. The interlobar pleura remains thickened, and the shadows of the perivascular lymphatics persist as fine, sharp lines, most marked at the bases and near the hila.

J. N. Ané, M.D.

LEAD POISONING

Lead Poisoning in Children. Charles F. McKhann and Edward C. Vogt. Jour. Am. Med. Assn., Oct. 7, 1933, CI, 1131–1135.

Lead poisoning in infants may follow the prolonged use of lead nipple shields; the use by the mother of face powder containing lead; the ingestion of water containing even small quantities of lead; the inhalation of lead fumes in cases in which storage battery casings are used as fuel; most frequently from the ingestion of lead as paint on articles the child puts in his mouth. Children appear to be more susceptible to severe intoxication than adults. Early symptoms are disturbed function of the gastro-intestinal tract and manifestations of anemia. More serious symptoms are peripheral neuritis and encephalitis.

Among the most useful aids in diagnosis are the zones of increased density at the growing ends of long bones and at the margins of the flat bones. These lines at the metaphyseal margins of the long bones are of greater density and width than usually seen in haleing rickets and accompanying Vitamin A deficiency. Spectroscopic examination of the cerebrospinal fluid or the blood will confirm the diagnosis very early. Quantitative determination of lead in the excreta, properly appraised, is acceptable as evidence.

C. G. Sutherland, M.D.

THE LIVER

The Color of the Urine following Roentgen and Radium Treatment. K. Herold and Hans Meissner. Strahlentherapie, 1933, XLVII, 291–308.

After administration of x-ray deep therapy the excretion of dyes in the urine is definitely increased. While this increase touches only the upper limit of the normal, this is exceeded considerably after exposure to radio-active substances. In both cases the increase lasts only a short period, a fact which may be explained by an injury to the liver or by an increased decomposition of erythrocytes.

Ernst A. Pohle, M.D., Ph.D.

PROTECTION AGAINST RADIATION

A Simple Ionometer for the Measuring of Protection in X-ray Laboratories. Kurt Leistner. Strahlentherapie, 1933, XLVII, 551.

This is a description of a specially constructed ionometer to permit determination of the amount of exposure received by the personnel in x-ray laboratories. It is possible, for instance, to carry a small ionization chamber in the pocket for a certain length of time and then determine the amount of r received during this interval.

Ernst A. Pohle, M.D., Ph.D.

RADIATION EFFECTS

The Leukocyte Drop following Exposure to Very Soft Roentgen Rays. E. Wilhelmy and Ning Yü. Strahlentherapie, 1933, XLVII, 531.

Bucky has stated that, following the application of 5 per cent H.E.D. over 1 sq. cm. field, using roentgen rays produced at 6 K.V., with exposure time of 0.25 minute, there occurs a definite drop of the leukocytes. The authors studied this problem in 38 cases (6 K.V., half value layer in Al 0.02 mm., 300 r, 6 x 6 cm. field). Very careful counts did not reveal changes in the number of leukocytes beyond the normal fluctuations. Since the studies were undertaken in normal individuals, the authors state that it is possible that, under pathologic conditions, a definite reaction may occur.

ERNST A. POHLE, M.D., Ph.D.

Roentgen Epilation of the Heads of Children for Mycotic Diseases of the Hair. H. T. Schreus. Röntgenpraxis, April, 1933, V, 253–257.

It is well known that a rational therapy of mycotic infection of the hair depends on epilation. Mechanical epilation is usually not sufficient. Roentgen epilation marked progress in the treatment of this disease, because, not only is it painless, but it also leads to an atrophy of the follicle and papilla, which lasts a few weeks. The epilation by means of roentgen rays is even to-day not an easy and harmless task: in the author's opinion it is one of the most difficult tasks in roentgen therapy.

Irradiation of the head from three fields (two lateral and one posterior) is practised by him. Keeping unruly children quiet for a considerable length of time is often difficult: occasionally narcotics have to be used. Too highly filtered rays should not be used for epilation. He recommends 90 K.V., filtered by 0.5 mm. Al (only occasionally 1 to 2 mm. Al), the dosis necessary for epilation being from 350 to 375 r. An erythema does not occur after this amount of irradiation, but the epilation lasts about six weeks. Unfiltered rays are much more dangerous to the skin.

For measuring the dose, ionization chambers are to-day essential. Areas of permanent alopecia must make one suspect error in technic; large areas of alopecia must always be so attributed. In these cases telangiectasis, atrophy, and pigmentation of the skin are other evidences of it. Only an expert should undertake epilation by roentgen rays. As after-treatment the author recommends a tincture of iodine (from 1 to 2 per cent), applied daily, and sulphur paste (from 15 to 20 per cent), with salicylic acid (from 2 to 3 per cent). A second roentgen treatment should never be given until six months have passed.

In about 30 per cent of the cases the epilation is unsatisfactory, and thallium is used. The latter is used also in children under three years of age: in their cases, a combined thallium and roentgen epilation is suggested. It seems that one can get a good epilation if he uses a little more than half of both these factors; that is, about 4.5 mgm. per kilogram of body weight of thallium and from 175 to 200 r per field.

H. W. HEFKE, M.D.

RADIATION INJURIES

Late Reactions on Human Skin following Roentgen Exposure Thirty-six Years Ago. Leopold Freund. Strahlentherapie, 1933, XLVII, 88.

The author reports three interesting cases, showing late reactions following roentgen exposure. The first patient is the individual with *Naevus pigmentosus piliferus* upon whom roentgen rays were used therapeutically for the first time in history. He was five years old at that time and was treated over the neck and the lumbar area. Examination this year showed that epilation had been permanent but there was also an ulcer 3 × 5 cm. at the site of the previous severe acute roentgen reaction produced at the time of treatment. In another case, roentgen epilation was carried out in a woman because of superfluous hair in the chin and both cheeks. Re-examination thirty-two years later showed absence of hair and no sign of atrophy, pigmentation, or other changes due to irradiation. The author feels that, in view of this observation, one should reconsider the epilation by roentgen rays for cosmetic purposes with the help of our modern dosage instruments. In a third case, treated in 1899 because of favus in the scalp, there were several areas of alopecia left, corresponding to the site of the original lesion.

ERNST A. POHLE, M.D., Ph.D.

RADIATION SICKNESS

The Pathogenesis of Roentgen Sickness. Elisabeth Willms. Strahlentherapie, 1933, XLVII, 503.

In a previous paper the author reported that cholesterol in the serum changed under roentgen exposure. There were definite correlations between cholesterol content and x-ray sickness. In the present article it is shown that in cases of x-ray sickness the acetone in the blood as well as the β-oxybutter acid are definitely increased. The amount of increase is dependent upon time and applied dose. It is at a maximum after irradiation of organs well supplied with blood.

ERNST A. POHLE, M.D., Ph.D.

RADIUM

Permanent Sterilization by Radium. P. Jonen. Strahlentherapie, 1933, XLVII, 309–321.

Permanent sterilization by roentgen rays is obtained by a complete destruction of the ovarian function;

secondarily there is an atrophy of the intra-uterine mucosa. Following intra-uterine radium application permanent sterilization is due to a direct effect on the endometrium, combined with an injury of the ovarian function. This disturbance of the latter is a necessity in the case of roentgen treatment but not necessary if radium is used. In order to reduce the menopausal symptoms the author suggests that one may pull the uterus downward during the time of radium application in order to decrease the dose effective in the ovaries. He has tried this method in eight patients, but, since the period of observation has been only eight months, he cannot make definite statements as to its efficacy.

ERNST A. POHLE, M.D., Ph.D.

ROENTGEN RAYS (MEASUREMENT)

Measuring the Quality of Roentgen Rays. H. Holthusen and R. Braun. Strahlentherapie, 1933, XLVII, 263–273.

In Germany the half value layer in aluminum and copper has been generally accepted as the quality factor in x-ray therapy. The International Congress in Paris (1931) also adopted it. A number of investigators, particularly in the United States, do not agree with this resolution, and Holthusen outlines in this article all points in favor of the half value layer.

ERNST A. POHLE, M.D., Ph.D.

SCURVY (INFANTILE)

Roentgenographic Visualization of Subperiosteal Hemorrhage in Infantile Scurvy. Waldo E. Nelson, William M. Doughty, and A. Graeme Mitchell. Jour. Am. Med. Assn., July 1, 1933, CI, 14–17.

Increased density at the end of the diaphysis, increased density around the epiphyseal centers (rimming of the nucleus of ossification in the epiphysis), ground-glass appearance of the shaft of the diaphysis and of the body of the epiphysis, thinning of the cortex of the diaphysis, lateral spurs at the end of the diaphysis, and epiphyseal separation (separation of the metaphysis) can usually be seen on the roentgenogram before the occurrence of subperiosteal hemorrhage. Kato believes that the last mentioned is the one sign that is absolutely unique in infantile scurvy. While not, therefore, an early or even a necessary sign of scurvy, subperiosteal hemorrhage is more characteristic than any other. The inner surface of the periosteum is frequently lined with newly formed bone which, in the course of healing, becomes heavier and is readily observed in the roentgenogram. This periostitis ossificans may result in the clot being surrounded by a perfect shell of bone, with bony columns penetrating the deeper layers. As healing takes place, the hematoma gradually becomes organized and calcification sets in. Unless serial roentgenograms are taken after treatment, subperiosteal hemorrhage may be entirely overlooked.

C. G. SUTHERLAND, M.D.

SILICOSIS AND PNEUMONOCONIOSIS

Silicon Dioxide Content of Lungs in Health and Disease. William D. McNally. Jour. Am. Med. Assn., Aug. 19, 1933, CI, 584–587.

The normal lung contains 1.13 mg. of silicon dioxide per gram of dried tissue. The lungs of tuberculous subjects contain somewhat more of silicon dioxide than do those of normal persons; some of this may come from inhalation or directly from the blood stream, as the blood of tuberculous subjects contains more silicon dioxide than does that of normal persons. All clinical observations have shown that a silicotic patient is particularly liable to fall a victim to a tuberculous infection and that the silicotic process continues to advance after complete withdrawal from exposure. During life, the diagnosis of silicosis depends on the history, clinical examination, and roentgenographic evidence of the disease. Many times the roentgenograms are not decisive, so that the diagnosis of silicosis, tuberculosis, or tuberculo-silicosis is not made with certainty. At autopsy the doubt may still linger and it is then that a chemical examination for the quantitative determination of silicon dioxide aids one in arriving at the correct diagnosis.

C. G. SUTHERLAND, M.D.

Etiology of Silicosis. A. J. Lanza. Jour. Am. Med. Assn., Aug. 19, 1933, CI, 583, 584.

Silicosis is a disease due to breathing air containing silica (SiO_2), characterized anatomically by generalized fibrotic changes and the development of miliary nodulation in both lungs. Clinically it is characterized by shortness of breath, decreased chest expansion, lessened capacity for work, absence of fever, increased susceptibility to tuberculosis (some or all of which symptoms may be present), and by characteristic x-ray findings. Committees of the American Public Health Association adopted this definition. The primary cause is free silica, inhaled in the form of dust, the dust particles being not less than 10 microns in their greatest diameter. Most of the dust penetrating the alveoli is less than 5 microns in diameter. A technic has been defined and standardized by the United States Public Health Service for sampling and counting. Dust concentrations are measured in terms of million particles per cubic foot.

Silicosis develops slowly, the rate of development depending largely on the dosage of silica, and this in turn is determined by three variables—the amount of dust in the inspired air, the amount of silica in the dust, and the extent of the exposure.

Certain substances present in silica-containing dust but not in combination with the silica, may advance or retard the development of silicosis. The presence of clay and other inorganic substances has been stated to prevent the development of silicosis, while in other instances certain alkalies are credited with greatly speeding up silicosis. The distinguishing characteristic of silicosis is the extraordinary susceptibility to tuberculosis which it induces in its victims. When a tuberculous infection is implanted on a silicotic lung, it intensifies and accelerates the formation of fibrotic tissue, and the pathologic vicious circle thus set up may continue for some time before the infection becomes clinically manifest. Pre-existent pulmonary disease, especially tuberculosis and pneumonoconioses other than silicotic, tend to hasten and aggravate the development of silicosis. Syphilitics develop silicosis more quickly and the disease runs a more rapid course. Negroes contract silicosis in a shorter time, with a quicker fatal termination, than do white men. Sandblasting offers a most serious hazard, and foundries and potteries contribute their quota of cases, as do processes involving grinding and vitreous enameling.

C. G. SUTHERLAND, M.D.

The Clinical Manifestations of Silicosis. R. R. Sayers. Jour. Am. Med. Assn., Aug. 19, 1933, CI, 580–583.

The disease has been divided, both in South Africa and the United States, into two classes: simple silicosis and silicosis plus tuberculosis, or tuberculosis with silicosis. Simple silicosis is further divided (for convenience of description and possible compensation purposes) into three stages: first, second, and third stage silicosis. In South Africa and in Ontario they are defined by law as anteprimary, primary, and secondary.

The earliest specific indication of the presence of silicosis is the radiographic appearance, consisting of generalized arborization throughout both lung fields, with more or less small, discrete mottling. This mottling is due to shadows cast by the discrete individual nodules of fibrous tissue in the lungs.

In the second stage there is a generalized medium-sized mottling through both lung fields. The shadows of the individual nodules are for the most part discrete and well-defined on a background of fibrous arborization, but there may be here and there larger but limited opacities due to irregular pleural thickening or to a localized aggregation of nodules.

The radiographic appearances in the third stage are further accentuated, the mottling is more intense, and the nodules are larger and take on a conglomerate form, so that large shadows are shown corresponding to areas of dense fibrosis.

C. G. SUTHERLAND, M.D.

Cancer of the Lungs among Uranium Miners. Prague letter, Jour. Am. Med. Assn., Aug. 19, 1933, CI, 618.

The lung cancer of Joachimstal continues to attract attention. The disease was known for many years among the miners in Schneeberg in Saxony but was described only a few years ago among the miners of the uranium mines in Joachimstal, from which radium is being produced. A commission was set up by the Czechoslovakian government to investigate this disease and its work was endowed by a grant from the president of the republic. The committee ascertained that this disease has been prevalent for many years in this mine but was not diagnosed as such, the high mortality among the miners being attributed to tuberculosis. It was found that half the deaths among the miners of Joachimstal can be attributed to cancer of the lungs. The disease appears among the miners only after many years of work in this region and the average age of those who die of lung cancer does not differ materially from that of those who die of other causes. The average age of both these groups is about 53 years. The investigative work of the committee was hampered by the attitude of the miners and their families, who refused to submit to periodic examinations and necropsies in case of death. To obviate this, a special ministerial decree was issued which authorizes the chief physician of the miners' insurance to enforce a physical examination of the miners. A special bonus is given to the family of a miner who has died of lung cancer in order to obtain consent for a necropsy. The disease has been put on the list of the occupational diseases that fall under the workmen's compensation act. Besides this, a special law is being prepared in the ministry of health which will regulate the preventative measures during the process of fabrication of radium and during its use for therapeutic purposes.

C. G. SUTHERLAND, M.D.

The Pathologic Reaction in Various Pneumonoconioses. Leroy U. Gardner. Jour. Am. Med. Assn., Aug. 19, 1933, CI, 594–598.

The forms produced by pure chemical substances tend to fall into three categories: predominantly linear, nodular, or diffuse in character. A linear pattern characterizes the general type of response to most inhaled inert foreign materials. Nodular lesions are apparently confined to silicosis, while diffuse reaction is exemplified in asbestosis. Mixed patterns are produced by dusts such as granite, which is composed of several different elements. The stages in the reaction to these well-known dusts are analyzed in an

attempt to explain the variations in the resultant pathologic picture. This can be done most concisely by considering in turn the various anatomic structures involved.

The processes of phagocytosis, lymphatic elimination, and involvement of the lymphoid tissue and pulmonary parenchyma are discussed in detail, as is the subject of mixed dusts.

C. G. SUTHERLAND, M.D.

Roentgenologic Aspect of Pneumonoconiosis and its Differential Diagnosis. Henry K. Pancoast and Eugene P. Pendergrass. Jour. Am. Med. Assn., Aug. 19, 1933, CI, 587–591.

Pulmonary fibrosis is the essential and characteristic feature of pneumonoconiosis in general, but in reality this is the terminal effect. Intermediate changes are of very considerable importance—those histologic changes which are the result of phagocytosis of dust particles and their introduction into the lymphatic system of the lungs. There is another industrial type in which the presence of asbestos bodies and their obstructive tendencies in the terminal air passages and the probable resulting minute atelectases are responsible for an important part of the clinical and pathologic features of the condition. Similar bodies have been found in the lungs of anthracotic individuals. The processes of cell proliferation and infiltration, lymph block, cell necrosis, and the factors in predisposition to infections must be given due consideration.

The first stage may closely simulate passive congestion as a result of cardiac decompensation, or associated with coronary thrombosis; advanced bilateral bronchiectasis; asthma; infiltrating or permeating malignant metastases; polycythemia or erythremia, or mycotic infections.

The early interstitial stage must be differentiated from a tuberculous pneumonic process in the rapidly developing cases, an interstitial pneumonitis, or bronchosinusitis or rheumatic pulmonitis.

The nodular phase may be simulated by tuberculosis of the perinodular silico-tuberculosis type, tuberculous bronchopneumonia, miliary tuberculosis, nodular metastatic malignant conditions of the lungs, actinomycosis, sporotrichosis, or leptothrix infection.

The advanced diffuse, or terminal fibrotic, stage is to be differentiated mainly from chronic diffuse tuberculosis or, occasionally, from mediastinal tumor.

The authors have seen three cases of primary bronchogenic carcinoma in association with pneumonoconiosis.

C. G. SUTHERLAND, M.D.

THE SKIN (THERAPY)

Studies of the Effects of Roentgen Rays on the Skin in Rabbits. F. Ellinger. Strahlentherapie, 1933, XLVII, 517.

The author has studied extensively the effect of roentgen rays (100 K.V., 6 ma., 2 mm. Al, half value layer in copper 0.16 mm.) on the ear of rabbits. The reaction, divided into four stages, is similar to that in human skin but is not identical with erythema or pigmentation. From 1,500 to 2,000 r are required to produce an erythema with epilation. It is concluded, therefore, that the skin of rabbits has 2.5 times the tolerance of human skin for roentgen rays. The author believes, therefore, that this can be used as a basis for transferring the results of animal experiments to human biology and pathology.

ERNST A. POHLE, M.D., Ph.D.

THE SKULL (THERAPY)

Diagnosis and Treatment of Injuries of the Head. Walter E. Dandy. Jour. Am. Med. Assn., Sept. 2, 1933, CI, 772–775.

Roentgenograms of the skull are of almost no service in acute injuries of the head; they are a waste of money, a misdirection of diagnostic effort, and only too frequently, if transportation is required, a critical tax on a seriously ill patient. It is only in the better disclosure of depressed fractures of the skull—the one most important concern in the bone—that x-rays are helpful, but even here inspection and palpation are almost as satisfactory.

C. G. SUTHERLAND, M.D.

THE SPINE

A Benign Form of Osteomyelitis of the Spine. Alan De Forest Smith. Jour. Am. Med. Assn., July 29, 1933, CI, 335–337.

Sixteen cases have been collected from the records of the New York Orthopedic Dispensary and Hospital or by orthopedists of recognized standing elsewhere. One other was seen in consultation. The vertebral bodies were involved in 14 and the posterior arches in three. The average age at the onset of the infection was 29.5 years. The lesions extended from the fifth dorsal to the fifth lumbar vertebra and tended to be grouped in the mid-dorsal or the mid-lumbar region. One patient had two separate foci of infection in the spine and another had three. These infections commonly follow others in different parts of the body for which the patient has been confined to bed, and when backache is complained of it is thought to be from some unimportant cause and no more attention is paid to it. In 11 of these a diagnosis of tuberculosis of the spine was made. Suspicion that these lesions were caused by some other infection was aroused by the fact that they followed, or in one or two cases preceded, pyogenic lesions in other parts of the body. The diagnosis was further supported by evidence of a productive bone reaction about the lesion and tendency for early bony ankylosis of the bodies. The onset was sudden in 13 cases and gradual in four. In all, pain (not relieved by

rest) was the outstanding symptom. One of the earliest evidences of osteomyelitis in the roentgenogram is a thinning of the intervertebral disc. A slight haziness and indistinctness of the bone structure also may occur quite early. A fusiform paravertebral abscess shadow is to be seen in the roentgenogram. Somewhat later, productive bone changes usually are seen about the periphery of the bodies and across the margins of the intervertebral space. There is a strong tendency for bony fusion of the bodies to take place. This mild form may easily be mistaken for tuberculosis.

C. G. SUTHERLAND, M.D.

THE THORAS

Tularemic Pneumonia: Report of Case. James R. Gudger. Jour. Am. Med. Assn., Oct. 7, 1933, CI, 1148–1150.

This is a report of a case that terminated fatally, though two cases have been reported in which the patient recovered. Fourteen fatal cases, with postmortem observations, have been reported. Twelve out of thirteen showed intrathoracic lesions of tularemia: eight of the thirteen showed definite inflammatory processes of pneumonia. Various authors estimate the mortality of all cases of tularemia to be about 4 per cent. The exact route by which the infection reaches the lungs, whether through the blood stream, lymphatic channels, or the respiratory passages, is unknown.

C. G. SUTHERLAND, M.D.

The Roentgen Appearance of Edema of the Lungs; A Contribution to the Pathogenesis of Edema of the Lungs. Erich Zdansky. Röntgenpraxis, April, 1933, V, 248–253.

Roentgenologic examination shows that acute edema of the lungs attacks preferably portions of the lungs which are used more extensively for breathing and which have a more active arterial circulation. The transudate on the other side, based on passive congestion, is most often seen in the parts of the lungs which are used for breathing to a lesser extent and in which blood and lymph circulation is slowed down. Factors which determine the resorption of fluid from lung tissue (lymphatic system) seem to influence the accumulation of edema and transudate. Roentgen examination shows that the portions of the lung which are free from edema may show no signs of passive congestion, a fact which helps to indicate that other factors beside circulatory disturbances are the basis for edema of the lungs. It is occasionally possible to detect a clinically latent, slowly developing edema by roentgenologic examination. The roentgen appearance of edema of the lungs is anatomically based on the filling of alveoli with transudate and by the edematous swelling of the interstitial tissue; it changes according to the predominance of the one or the other factor. A few cases are reported.

H. W. HEFKE, M.D.

TUMORS (THERAPY)

Experience in the Treatment of Intrathoracic Tumors. R. Gantenberg. Strahlentherapie, 1933, XLVII, 426.

The author reports his observations on 16 cases of primary bronchiogenic carcinoma: 2 metastatic mediastinal carcinoma, 1 primary lung sarcoma, and 1 in the mediastinum (probably metastatic from struma or thymus). The treatment was given in series through three or four fields with 180 K.V., 4 ma., 0.5 mm. Cu + 1.0 mm. Al, 50–80 per cent H.E.D. to each field in each series. Repetition of the series after from six to eight weeks. In one case the Coutard method was used. In 5 out of 20 cases, a definite improvement was obtained. In some, the process came to a standstill for a period of years. This is a result which should lead one to give radiation therapy a trial in every case.

ERNST A. POHLE, M.D., Ph.D.

The Separate Position of the "Granulosakarzinom" of the Ovarium (Ovarialblastoma) from the Clinical, Histological, and Radiotherapeutic Standpoints. H. O. Kleine. Strahlentherapie, 1933, XLVII, 326.

The author reports 12 cases of "granulosakarzinom" (both of ovary) which were characterized by a continued function of the granulosa-epithelium. This manifests itself in stimulation of growth in breasts, myometrium, mucous membrane of the tubes and of the endometrium. The youngest case in the author's series was 3 years, 6 months old. Because of the histologic character of the cells the tumors are highly radiosensitive.

ERNST A. POHLE, M.D., Ph.D.

Results of Radiation Therapy in Carcinoma of the Uterus. H. Eymer. Strahlentherapie, 1933, XLVII, 119–124.

The author presents in a number of tables the end-results obtained in the radiation treatment of carcinoma of the uterus at the Women's Clinic, University of Heidelberg. During 1913–1932 a total of 893 cases of carcinoma of the cervix and 216 of carcinoma of the fundus were seen. For five-year statistics, 587 carcinomas of the cervix and 115 carcinomas of the fundus could be used in this report. Data on mortality and on radiation injuries are also given. The author has the impression that results of irradiation in carcinoma of

the cervix have improved during the last years. He also feels that further technical improvements are possible.

ERNST A. POHLE, M.D., Ph.D.

Roentgentherapy of Malignant Tumors with Short Focal Skin Distance. H. Chaoul and A. Adam. Strahlentherapie, 1933, XLVIII, 31–50.

In a well illustrated article, accompanied by tables with detailed clinical data, the authors report the results obtained by treating malignant tumors with heavily filtered rays (180 K.V., 0.5 Au) at short distance (8 cm. F.S.D.) and high doses (8,000 r in 21 days). Although only 25 months have elapsed since the first case was treated and no final conclusions can be offered, the results appear to be so encouraging that investigation of this method by other workers is recommended. The advantage of this method in comparison with radium implantation of, for instance, tumors of the floor of the mouth, is seen in the avoidance of the danger of infection.

ERNST A. POHLE, M.D., Ph.D.

Experimental Tumors and Their Significance for the Study of Roentgen Effects, with a Contribution as to the Systemic Effect of Roentgen and Radium Rays. H. G. Zwerg. Strahlentherapie, 1933, XLVII, 485.

The author discusses the value of experimental tumors in radiation research. He briefly reports his own experiments, undertaken on rats, with the Jensen sarcoma. If from 190 to 360 r were given over the entire body, the tumor grew rapidly as compared with the untreated controls. If only from 90 to 120 r were applied, there was little or no difference between treated and untreated animals. Radium exposure gave essentially the same results. A definite influence of the time factor could be detected.

ERNST A. POHLE, M.D., Ph.D.

WOUNDS (THERAPY)

The Process of Healing in Inflammations under the Influence of Roentgen Rays. J. Tannenberg and L. Bayer. Strahlentherapie, 1933, XLVII, 408.

The author exposed one-half of skin wounds in rabbits with roentgen rays and found that healing is accelerated by the exposure. This effect is seen even if the wound is made from 3 to 20 hours after the exposure. The inflammatory process is not decreased by irradiation but merely accelerated; it starts earlier and leads to healing in a shorter time. The mechanism of the process is discussed in detail. The doses used amounted to 400 r (170 K.V., 0.5 mm. Zn).

ERNST A. POHLE, M.D., Ph.D.